FINAL BRIEF
[ORAL ARGUMENT NOT YET SCHEDULED]
No. 03-5020

IN THE UNITED STATES COURT OF APPEALS
FOR THE DISTRICT OF COLUMBIA CIRCUIT

JULIAN M. WHITAKER, et al.

Plaintiffs-Appellants,

v.

TOMMY G. THOMPSON, Secretary,
U.S. Department of Health and Human Services, et al.,

Defendants-Appellees.

ON APPEAL FROM THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

BRIEF FOR THE FEDERAL APPELLEES

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CERTIFICATE as to Parties, Rulings, and Related Cases
(Cir. R. 28(a)(1))

1. Parties and Amici below:

   The plaintiffs were Julian M. Whitaker, M.D.; Pure Encapsulations, Inc.; Durk Pearson and Sandy Shaw; and the American Association for Health Freedom.

   The defendants were Tommy G. Thompson, Secretary of Health and Human Services; the United States Department of Health and Human Services; Mark B. McClellan, M.D., Commissioner of Food and Drugs, Food and Drug Administration; and the United States Food and Drug Administration.

   There were no intervenors or amici in the district court.

2. Ruling under Review: The ruling under review is the Memorandum Opinion and Order of Judge Gladys Kessler filed January 3, 2003, 239 F. Supp.2d 43 (D.D.C. 2003) (JA 2174).

3. Related Cases: The instant case was not previously before this Court. Counsel for the appellees are unaware of any related cases within the meaning of Cir. R. 28(a)(1)(C).

Howard S. Scher

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Cases:

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* Cases and authorities chiefly relied upon are marked with an asterisk.

Constitution:

Statutes:

Federal Food, Drug, and Cosmetic Act:

Regulations:

Rules:

Legislative Materials:

Miscellaneous:

Glossary

APA	—	Administrative Procedure Act
AR	—	Administrative Record
BPH	—	Benign prostatic hypertrophy
DSHEA	—	Dietary Supplement Health and Education Act of 1994
FDA	—	Food and Drug Administration
FDCA	—	Federal Food, Drug, and Cosmetic Act
JA	—	Joint Appendix
NLEA	—	Nutrition Labeling and Education Act of 1990
OTC	—	Over the counter

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Jurisdictional Statement

Plaintiffs challenged a final order of the Food and Drug Administration (FDA), invoking the district court's jurisdiction pursuant to 28 U.S.C. 1331. JA 1653 (Complaint ¶ 6). On January 3, 2003, the district court entered a final decision granting FDA's motion to dismiss and denying plaintiffs' motion for summary judgment. JA 2174. Plaintiffs filed a timely notice of appeal on January 6, 2003. JA 2199. See Fed. R. App. P. 4(a)(1). This Court has appellate jurisdiction under 28 U.S.C. 1291.

Issues Presented

1. Whether FDA properly denied plaintiffs' petition to authorize a proposed health claim for a dietary supplement because the claim was to treat an existing disease rather than to reduce the risk of developing a disease, which meant that the claim fell within the scope of the Federal Food, Drug, and Cosmetic Act's drug provisions and outside its health claims provisions.

2. Whether FDA's denial of plaintiffs' petition violated the First Amendment.

Statement of the Case

A. Nature of the Case.

At issue is plaintiffs' petition to market a dietary supplement containing saw palmetto extract and bearing the following claim: "Consumption of 320 mg. daily of Saw Palmetto extract may improve urine flow, reduce nocturia and reduce voiding urgency associated with mild benign prostatic hyperplasia (BPH)." Previously, in 1990, FDA issued a final rule banning from the market over-the-counter drugs containing saw palmetto that were sold to treat these same symptoms of BPH because saw palmetto was not safe or effective to treat these symptoms. 55 Fed. Reg. 6926 (1990).

In 1999, rather than submit an application for approval of a new drug, or a citizen's petition seeking reconsideration of the 1990 final rule, plaintiffs submitted

a petition seeking FDA's authorization of the above-mentioned claim for use on a dietary supplement under the health claims provision of the Nutrition Labeling and Education Act of 1990 (NLEA), 21 U.S.C. 343(r)(5)(D). FDA denied the petition, concluding that the Federal Food, Drug, and Cosmetic Act (FDCA) does not permit FDA to authorize as a "health claim" a statement that a substance has a therapeutic effect on an existing disease. In FDA's view, the FDCA permits only health claims that speak to the reduction of the risk of developing a disease (or condition) or the long-term prevention of a disease, not the treatment of an existing disease. Under FDA's long-held view, a claim that a product treats a disease renders it a drug subject to the drug provisions of the statute. Permitting dietary supplements to make such claims without being subject to those provisions would therefore allow an end-run around the extensive drug-approval provisions of the FDCA which are designed to ensure that drugs are safe and effective for their intended uses. Plaintiffs challenged FDA's denial on statutory and constitutional grounds. FDA moved to dismiss for failure to state a claim, and plaintiffs moved for summary judgment. The district court granted FDA's motion.

B. Statutory And Regulatory Background.

The pertinent statutory and regulatory provisions are included in the Addendum to this brief.

The FDCA, in pertinent part, establishes a scheme for the regulation of food and drugs. The touchstone for determining whether an item is a drug and to be regulated as such is the drug definition in 21 U.S.C. 321(g)(1). Under subsection (B) of that provision, the pertinent provision in this case, a "drug" is any "article[] intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease in man or other animals * * *." Under this definition, therefore, foods can be drugs depending on their intended uses and, as a result, regulated as drugs. See, e.g., Gadler v. United States, 425 F. Supp. 244, 246 (D. Minn. 1977) ("even the most commonly ingested foods and liquids are 'drugs' within the meaning of the Act if their intended use falls within the definition of § 321(g)(1)(B)") (citing cases).

1. In the mid-1980s, claims on foods relating to disease and health increased dramatically. In 1987, in response, FDA proposed regulations designed to allow food manufacturers to make limited types of disease-specific claims in labeling without being subject to the regulatory requirements for drugs. 52 Fed. Reg. 28,843 (1987); 55 Fed. Reg. 5176 (1990) (re-proposal). At that time, dietary supplements were regulated either as "food" (see 21 U.S.C. 321(f)) or as a "drug" (see 21 U.S.C. 321(g)(1)), depending on their intended uses. Slip op. 2-3 (JA 2175-76). If a disease-specific claim were made regarding a dietary supplement, the supplement was regulated as a "drug," rather than as a food. See 56 Fed. Reg. 60,537 (1991).

healthy dietary practices by providing them valid information through claims "supported by a significant scientific agreement," while also protecting consumers from fraud and misleading information. Id. at 8-10.

To that end, the NLEA amended the FDCA by allowing claims to be made, under certain conditions, "in the label or labeling of the food which expressly or by implication * * * characterize[] the relationship of any nutrient * * * to a disease or a health-related condition * * *." 21 U.S.C. 343(r)(1)(B)[2]; see also 21 C.F.R. 101.14(a)(1) (defining "health claim").[3] Health claims, however, must be made in accordance with 21 U.S.C. 343(r)(3) (pertaining to conventional food) or § 343(r)(5)(D) (pertaining to "a dietary supplement of vitamins, minerals, herbs, or other similar nutritional substances"). Under 21 U.S.C. 343(r)(3)(B)(i), a health claim may be made with respect to food only if FDA has determined in a regulation that,

> based on the totality of publicly available scientific evidence (including evidence from well-designed studies conducted in a manner which is consistent with generally recognized scientific procedures and principles), * * * there is significant scientific agreement, among experts qualified by scientific training and experience to evaluate such claims,

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[2] The FDCA defines "label" as "a display of written, printed, or graphic matter upon the immediate container of any article * * *," and "labeling" means "all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article." 21 U.S.C. 321(k), (m).

[3] The NLEA pertains solely to labeling (not to any other form of promotion) and does not restrict the sale of any products.

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1. In the mid-1980s, claims on foods relating to disease and health increased dramatically. In 1987, in response, FDA proposed regulations designed to allow food manufacturers to make limited types of disease-specific claims in labeling without being subject to the regulatory requirements for drugs. 52 Fed. Reg. 28,843 (1987); 55 Fed. Reg. 5176 (1990) (re-proposal). At that time, dietary supplements were regulated either as "food" (see 21 U.S.C. 321(f)) or as a "drug" (see 21 U.S.C. 321(g)(1)), depending on their intended uses. Slip op. 2-3 (JA 2175-76). If a disease-specific claim were made regarding a dietary supplement, the supplement was regulated as a "drug," rather than as a food. See 56 Fed. Reg. 60,537 (1991).

Based on comments to the 1987 proposal, agency experience while the proposed rule was pending, and advances in knowledge about the relationship between diet and health, FDA concluded that the 1987 proposal was too broad and could lead to uncertainties that might lead to fraud. Accordingly, FDA issued a narrower proposal in 1990. 55 Fed. Reg. 5176 (1990). Both proposed rules, as well as the scientific publications cited to support them, focused on diet as a means of reducing the risk of developing a disease or forestalling the premature onset of chronic diseases, such as cancer and coronary heart disease. 52 Fed. Reg. at 28,845 (col. 3); 55 Fed. Reg. at 5192 (col. 1). See also AR 722-23 (JA 731-32).

Before these rules were finalized and because unsubstantiated health claims were becoming commonplace, Congress passed the NLEA in 1990. See 136 Cong. Rec. H12,953 (1990) (AR 775; JA 784).[1] A principal purpose of the NLEA was to "provide[] a process for the orderly regulation of disease claims" for foods, in which FDA "would review the scientific evidence and decide if the claim is valid. A disease claim may not be made unless it is consistent with a final regulation issued by the FDA." H.R. Rep. No. 101-538, at 8 (1990) ["House Report"], reprinted in 1990 U.S.C.C.A.N. 3336, 3337. The legislation was intended to help consumers maintain

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[1] The NLEA also imposed other requirements concerning the labeling of nutrients in foods. See Arent v. Shalala, 70 F.3d 610 (D.C. Cir. 1995).

healthy dietary practices by providing them valid information through claims "supported by a significant scientific agreement," while also protecting consumers from fraud and misleading information. Id. at 8-10.

To that end, the NLEA amended the FDCA by allowing claims to be made, under certain conditions, "in the label or labeling of the food which expressly or by implication * * * characterize[] the relationship of any nutrient * * * to a disease or a health-related condition * * *." 21 U.S.C. 343(r)(1)(B)[2]; see also 21 C.F.R. 101.14(a)(1) (defining "health claim").[3] Health claims, however, must be made in accordance with 21 U.S.C. 343(r)(3) (pertaining to conventional food) or § 343(r)(5)(D) (pertaining to "a dietary supplement of vitamins, minerals, herbs, or other similar nutritional substances"). Under 21 U.S.C. 343(r)(3)(B)(i), a health claim may be made with respect to food only if FDA has determined in a regulation that,

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that the claim is supported by such evidence.

Under Section 343(r)(5)(D),

> [a health] claim made with respect to a dietary supplement of vitamins, minerals, herbs, or other similar substances shall not be subject to subparagraph (3) [conventional foods] but shall be subject to a procedure and standard, respecting the validity of such claim, established by regulation of [FDA].

If a claim is not made in accordance with these procedures, the product is an unapproved new drug and "misbranded," and subject to seizure. 21 U.S.C. 355, 352(f), 343, 334. The misbranding of a food or a drug is a prohibited act, as is the introduction of an unapproved new drug into interstate commerce, and is subject to injunctive relief and other penalties. 21 U.S.C. 331(b), (d) ("Prohibited acts"), 332, 333.

With respect to health claims made under § 343(r)(3) (conventional foods), the NLEA authorizes persons to petition FDA to issue a regulation to authorize the health claim. 21 U.S.C. 343(r)(4). By regulation, FDA adopted the same petition procedure for dietary supplement health claims made under § 343(r)(5)(D). 21 C.F.R. 101.70. A party wishing to obtain a regulation authorizing a dietary supplement health claim must submit a petition with the proposed health claim, accompanied by supporting scientific evidence. FDA must then notify the applicant within 100 days whether the request will be denied or else "file[d] * * * for further action by [FDA]." If further

review is warranted, within the next 90 days FDA must either deny the petition or publish a proposed regulation authorizing the health claim. If FDA publishes a proposed rule authorizing a health claim, the agency must publish a final regulation approving or denying the claim within 270 days of publication. 21 C.F.R. 101.70(a)-(i), (j)(2)-(4). Under the NLEA, therefore, a health claim for a dietary supplement is not automatically subject to the FDCA's drug provisions so long as the claim is made in accordance with 21 U.S.C. 343(r)(5)(D) and other applicable sections of the FDCA. See also § 321(g) (penultimate sentence).

2. Following enactment of the NLEA, FDA undertook the task of developing regulations to implement the health claim process and to appropriately distinguish among conventional foods and dietary supplements (on the one hand) and drugs (on the other), as required under the FDCA as amended by the NLEA. Throughout, FDA consistently distinguished between nutritional effects of food substances, which would be an appropriate subject for a health claim, and effects that are pharmacological, therapeutic, or medicinal, which would not. See, e.g., 56 Fed. Reg. at 60545-46; 58 Fed. Reg. 2478, 2501 (col. 3) (1993); 59 Fed. Reg. 395, 408 (col. 3) (1994). FDA considered the nature of the science supporting dietary effects on disease and Congress' expressed intent to allow conventional foods and dietary supplements to make certain disease-specific health claims without being subject to

the FDCA's requirements for drugs. FDA determined that the relationship of a food or food component to a disease is different from that of a drug because it is difficult to demonstrate causal associations between different dietary factors and particular diseases. Genetic, environmental, and behavioral factors in addition to diet affect the development of disease, and foods themselves are complex in that they can contain some factors that promote disease and other factors that are protective against disease. 58 Fed. Reg. at 2501-02. The agency further determined that most types of disease claims that appear on drugs would not be appropriate as health claims on foods because they "imply a degree of association between the substance and the disease that is not supportable for any food * * *." 56 Fed. Reg. at 60552 (col. 2). Moreover, "subject[ing] dietary supplements to the same standard that applies to food in conventional form * * * strikes the appropriate balance between the congressional concern for consumer protection [from] fraud, public health, and sound science, on the one hand, and the desire to provide the consumer with information on the other." 58 Fed. Reg. 33,700, 33,706 (cols. 2-3) (1993).[4] With respect to botanicals like saw palmetto, for example, FDA stated as follows:

> [T]here is no basis under the act for FDA to permit health claims for

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[4] See also 58 Fed. Reg. at 33,702 (col. 1) (FDA noted that, with respect to health claims, Congress had "three broad areas of concern — consumer protection from fraud, sound scientific principles, and public health").

> herbs whose only known use is for medicinal effects. Health benefits of such herbs may appear in the labeling only in accordance with the drug provisions of the act. Where herbs have a history of use both as foods and drugs, the context of all of the available information on the intended use of the product will determine whether FDA will regulate the herbs as foods, as drugs, or as both foods and drugs.

58 Fed. Reg. at 2501 (col. 3) (emphasis added).

In its final rule, published in 1994, FDA stated that claims to "correct an abnormal physiological function caused by a disease or health-related condition" would be drug claims rather than health claims. 59 Fed. Reg. at 407 (col. 2). FDA further stated that:

> statements that a product may be effective in the cure, mitigation, treatment or prevention of disease will make the product a drug. However, statements that a product may reduce the risk of developing a disease or health-related condition may, or may not, make the product a drug. Exactly how a substance-disease relationship is to be characterized is one of the issues that the agency will address in deciding whether to authorize a health claim * * *. FDA advises that there is no provision in the act for the agency to exempt statements about symptoms of disease from causing products to be regulated as drugs. Although such statements may not be claims that the product will treat the disease that causes the symptoms, the statements clearly pertain to the mitigation of disease by addressing the symptoms caused by the disease.

59 Fed. Reg. at 412-13 (emphasis added).

The agency also adopted the "significant scientific agreement" standard applicable to health claims for conventional foods as the scientific standard for

evaluating health claims for dietary supplements. 59 Fed. Reg. at 400-06, 415-16. The regulation (which applies to all foods) provides:

> FDA will promulgate regulations authorizing a health claim only when it determines, based on the totality of publicly available scientific evidence (including evidence from well-designed studies conducted in a manner which is consistent with generally recognized scientific procedures and principles), that there is significant scientific agreement, among experts qualified by scientific training and experience to evaluate such claims, that the claim is supported by such evidence.

21 C.F.R. 101.14(c).[5]

3. In 1994, Congress enacted the Dietary Supplement Health and Education Act of 1994 (DSHEA) to create "a rational Federal framework * * * to supersede the current ad hoc, patchwork regulatory policy on dietary supplements" to protect consumers' right of access to "safe dietary supplements * * * to promote wellness." Pub. L. No. 103-417, § 2(15), 108 Stat. 4325 (1994). Among other things, the

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[5] In Pearson v. Shalala, 164 F.3d 650, 655 (D.C. Cir. 1999), this Court ordered FDA to further define the "significant scientific agreement" standard used in evaluating dietary supplement health claims. In response, FDA issued "Guidance for the Industry: Significant Scientific Agreement in the Review of Health Claims for Conventional Foods and Dietary Supplements." See <http://www.cfsan.fda.gov/~dms/ssaguide.html>. The Guidance states that "significant scientific agreement" means that "the validity of the relationship is not likely to be reversed by new and evolving science, although the exact nature of the relationship may need to be refined." Id. at 2. In addition, as a result of the Pearson decision, FDA permits qualified health claims through the exercise of enforcement discretion where the health claim does not meet significant scientific agreement if, inter alia, the claim can be made non-misleading with a disclaimer. See 67 Fed. Reg. 78002 (2002).

DSHEA defined "dietary supplement" and amended the definition of a "drug." Id. at §§ 3(a), 5, 108 Stat. at 4327, 4332.

The DSHEA defined a "dietary supplement," in pertinent part, as "a product (other than tobacco) intended to supplement the diet that * * * contains" a "dietary ingredient" such as, inter alia, "an herb or other botanical * * *." 21 U.S.C. 321(ff)(1)(C). As discussed below, Congress considered but rejected a proposal to exclude dietary supplements categorically from the FDCA's drug provisions. Instead, the DSHEA provided that "[e]xcept for purposes of [the drug definition in 21 U.S.C. 321(g)], a dietary supplement shall be deemed to be a food within the meaning of this chapter." 21 U.S.C. 321(ff) (last sentence).

The DSHEA also added § 343(r)(6) to the FDCA. That section specifically authorized certain types of claims about the uses of dietary supplements — including claims that previously would have required FDA review before the claim could be made — without triggering the health claim authorization provisions or the requirements applicable to drugs. 65 Fed. Reg. 1000, 1001 (2000) (col. 1). Claims permitted by § 343(r)(6) without prior FDA authorization include certain claims relating to the role of "a nutrient or dietary ingredient" intended to affect the structure or function of the human body and claims relating to general well-being from consumption of a nutrient or dietary ingredient. 21 U.S.C. 343(r)(6). These

"statements are generally referred to as 'structure/function claims.'" 65 Fed. Reg. at 1001 (col 2.). However, such claims "may not claim to diagnose, mitigate, treat, cure, or prevent a specific disease or class of diseases." 21 U.S.C. 343(r)(6). [6]

Under the statute, "drug" includes both "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals," 21 U.S.C. 321(g)(1)(B), and "articles (other than food) intended to affect the structure or any function of the body of man or other animals," 21 U.S.C. 321(g)(1)(C). The DSHEA created limited safe harbors from both of these parts of the drug definition. With respect to structure/function claims, the DSHEA amended the definition to state that "[a] food, dietary ingredient, or dietary supplement for which a truthful and not misleading statement is made in accordance with section 343(r)(6) of this title is not a drug * * * solely because the label or labeling contains such a statement." 21 U.S.C. 321(g)(1) (last sentence) (emphasis added). With respect to health claims, the DSHEA amended the "drug" definition to state that "[a] food or dietary supplement for which a claim, subject to * * * sections 343(r)(1)(B) and 343(r)(3) * * * or * * * 343(r)(5)(D) of this title, is made in accordance with the

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[6] One narrow statutory exception is that a dietary supplement health claim regarding "a classical nutrient deficiency disease" (such as "Vitamin C prevents scurvy") may be made without prior FDA authorization as long as the manufacturer "discloses the prevalence of such disease in the United States" and meets other requirements of 21 U.S.C. 343(r)(6).

requirement of section 343(r) of this title is not a drug solely because the label or the labeling contains such a claim." 21 U.S.C. 321(g)(1) (penultimate sentence) (emphasis added).

The DSHEA did not amend or modify the FDCA's drug provisions other than as specified above. The DSHEA also did not amend the FDCA's health claim provisions to change for dietary supplements the procedure or standard for premarket authorization of health claims that FDA adopted by regulation in 21 C.F.R. 101.14 and 101.70(a)-(i), (j)(2)-(4). Thus, the intended use of a "dietary supplement" remains central to determining whether a dietary supplement's claim will subject the product to regulation under the FDCA's drug provisions or the health claim (or other) provisions. See 65 Fed. Reg. at 1001 (col. 2).

C. Facts and proceedings to date.

1. On February 27, 1990, as part of its ongoing review of over-the-counter (OTC) drugs, FDA issued a final rule on benign prostatic hypertrophy (BPH) drug products, like saw palmetto. The rule applied to over-the-counter drug products labeled, represented, or promoted to relieve the symptoms of an enlarged prostate gland. FDA's final rule established that these products were not generally recognized as safe or effective, and were therefore unapproved new drugs and misbranded under the FDCA in the absence of an approved new drug application. Accordingly, since

August 27, 1990, the effective date of the rule, no over-the-counter product containing ingredients offered for use in relieving the symptoms of BPH may be marketed or sold. 21 C.F.R. 310.532. See also 55 Fed. Reg. at 6926-6930; AR 729 (JA 738).[7]

2. On May 25, 1999, plaintiffs filed a health claim petition with FDA seeking authorization for the labels of saw palmetto supplements (specifically, the n-hexane lipidosterolic extract of the pulp and seed (fruit) of the dwarf American palm, Serenoa repens) (Op. at 6 n.7; JA 2179) to include the following proposed health claim:

> Consumption of 320 mg daily of Saw Palmetto extract may improve urine flow, reduce nocturia and reduce voiding urgency associated with mild benign prostatic hyperplasia (BPH).

(AR 22) (JA 30). As required by regulation, plaintiffs included the scientific evidence they believed supported their claim. AR 121-397 (JA 129-405). Plaintiffs also requested that FDA "authorize the claim * * * with such disclaimer or disclaimers as the agency reasonably deems necessary to avoid a potentially

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[7] In the course of this proceeding, FDA also considered the possibility of a proposed warning to permit over-the-counter sales of BPH drugs: "Because this drug relieves only the symptoms of enlarged prostate without affecting the disease itself, periodic reexamination by a doctor is strongly recommended." In the end, however, the agency rejected that approach, concluding that "providing symptomatic relief without eliminating, arresting, or treating the obstructive causes of benign prostatic hypertrophy will mask the potential of the condition's progression and result in delayed diagnosis of secondary complications, i.e., stagnation of residual urine, urinary tract infection, and potential renal damage." 55 Fed. Reg. at 6929 (col. 2).

misleading connotation." AR 10 (JA 18).

Plaintiffs' petition was denied by operation of law on December 1, 1999, because FDA allowed 90 days to pass without issuing a decision. AR 710 (JA 719). FDA stated that the denial by operation of law was necessary because the prescribed time frame was insufficient to resolve "whether health claims for foods (including dietary supplements) may encompass [a claim of an effect on an existing disease] or whether such a claim is appropriate only on a product that has been shown to meet the safety and efficacy requirements for drugs." Ibid. The agency further stated that it would "seek public input on the important issue [the petition] raises" and would "reconsider" the petition. Ibid.

3. a. Plaintiffs filed the instant suit on December 7, 1999, seeking declaratory and injunctive relief. JA 1650. In pertinent part, plaintiffs argued that denial of their petition violated the FDCA, the Administrative Procedure Act (APA), and the First Amendment. The action was stayed pending FDA's reconsideration of its decision. JA 4 (Docket Entry No. 11).

b. On April 4, 2000, FDA held a public meeting to consider, among other things, whether claims about an effect on an existing disease may be made as health claims, or whether such claims are necessarily drug claims. AR 722, 729, 793-923 (JA 731, 738, 802-932). At the meeting, a physician representing the American

Urological Association (AUA) expressed views consistent with those stated in the 1990 final rule on over-the-counter drug products for BPH use. The AUA representative, Dr. Holtgrewe, testified that the lower urinary tract symptoms in older men associated with BPH (urinary frequency, urinary urgency, slowing of the urinary stream, hesitation on initiation of urination, getting up several times during the night to urinate) "are symptoms of disease, not a normal process of aging" and that, "among the diseases that produce such symptoms are life-threatening cancers, e.g., cancer of the prostate and cancer of the urinary bladder." AR 729 (JA 738).[8] The AUA's concern was that men experiencing the lower urinary tract symptoms associated with BPH "may self-medicate" and "thus delay timely and accurate diagnosis of their cancers," which "can rarely be cured once they have spread beyond the confines of the bladder and prostate." AR 729-30 (JA 738-39). Early diagnosis is essential. Therefore, dietary supplements marketed for symptoms of BPH may cause "irreparable harm" when men with cancer lose precious time by self-medicating under the illusion that they are treating a benign, non-life-threatening condition. Transcript of Hearing, AR 873-75, 886-896 (JA 882-84, 895-905). See also AR 729-730 (JA 738-39).

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[8] See also AR 1558-59 (Merck Manual listing BPH as a "genitourinary disorder") (JA 1568-69); and AR 1561 (1997 medical journal article describing BPH as "a common cause of morbidity among older men") (JA 1571).

c. On May 26, 2000, FDA issued its decision, denying plaintiffs' petition. (AR 721-732) (JA 730-741). FDA explained that historically all the health claims it had authorized since passage of the NLEA were claims "about reducing the risk of contracting a particular chronic disease," not "claim[s] about the an effect on an existing disease * * *." AR 721 (JA 730). FDA then undertook an exhaustive review of the statute and the legislative history (as well as its prior interpretations of claims to treat diseases), see AR 723-730 (JA 732-39), and concluded that "claims about effects on existing diseases do not fall within the scope of the health claims provisions in 21 U.S.C. § 343(r) and therefore may not be the subject of an authorized health claim" under the express terms of the statute (AR at 723; JA 732).

This understanding was further supported by the medical foods provisions in the statute. 21 U.S.C. 360ee(b)(3). See AR 729 (JA 738). Congress, FDA noted, created a medical foods provision to address the nutritional or "dietary management of disease" (ibid.). Therefore, Congress distinguished the "ordinary food supply" from medical foods by targeting the health claims that ordinary foods can make at "non-diseased people" (ibid.). That "clear separation," moreover, "recognizes that the diseased populations * * * are particularly vulnerable by virtue of having the disease" and that, accordingly, a food that carries claims regarding disease treatment or management should be regulated as a drug unless it is a medical food (ibid.).

Focusing on plaintiffs' proposed claim, FDA found that it was "directed at men who have already contracted BPH" (AR 721-22; JA 730-31), and thus can be "characterized as a claim to treat disease, a claim to mitigate disease, or both" (AR 722; JA 731). See also AR 728 (JA 737) (plaintiffs' "petition clearly identifies the intended use of saw palmetto extract products bearing that proposed claim as the treatment of the urinary symptoms of BPH" which "establishes the intended use of products bearing the claim as drugs"). Since the proposed claim concerned disease treatment, it was a drug claim and could not be considered a health claim. Accordingly, FDA denied the petition. AR 731 (JA 740).

In addition to the statutory language and legislative history, FDA noted that its understanding of the statute was supported by public health risks associated with allowing dietary supplements to make claims regarding the treatment, mitigation, or management of disease. First, in 1990, FDA had rejected the use of saw palmetto to treat the symptoms of BPH in the over-the-counter drug context because of health risks. AR 729 (JA 738). FDA had concluded that the clinical studies testing saw palmetto did not provide "sufficient evidence of effectiveness, i.e., adequate and meaningful clinical improvement" in treating the symptoms of BPH. Ibid. (internal quotation marks and citations omitted). It was concerned that "men with BPH may be lulled into a false sense of security and postpone reexamination by a physician,

resulting in delay in treatment of the disease," which "could result in delayed diagnosis of secondary complications such as stagnation of residual urine, urinary tract infection, and potential renal damage." Ibid., citing 55 Fed. Reg. at 6929. As also noted above, similar concerns had been raised at the April 4, 2000, hearing by the American Urological Association, whose representative testified that prostate and bladder cancer can produce symptoms similar to symptoms of BPH, that self-medication for BPH could "delay timely and accurate diagnosis of their cancers," and that these cancers "can rarely be cured once they have spread beyond the confines of the bladder and prostate." AR 729-30 (JA 738-39).

Second, FDA believed that a contrary interpretation would not only be inconsistent with the wording of the statute but would undermine "the public health protections of the statutory and regulatory requirements for drugs" in two ways. AR 730 (JA 739). One, because many pharmacologically active substances are botanicals and have possible uses in disease treatment, they would avoid drug regulation since they could qualify as dietary ingredients for use in dietary supplements (see 21 U.S.C. 321(ff)(1)). This would mean that such substances would avoid the "stringent safety and efficacy standards" applicable to both prescription and over-the-counter drugs. AR 730 (JA 739). Two, because "[a]pproximately 94% of prescription drugs" and "almost all OTC drugs for disease uses" are offered to treat disease, rather than to

prevent disease, it is "unlikely that manufacturers would seek drug approval from FDA for any product containing a substance that could be characterized as a dietary supplement or conventional food component, but rather would take the health claim route." Ibid. The protections of the drug approval system and other regulatory requirements applicable to drugs would thus be lost for a large number of products used to treat disease. Ibid.

d. After the decision, proceedings in this case recommenced. Plaintiffs moved for summary judgment, and the government moved to dismiss for failure to state a claim. The district court granted the government's motion, denied plaintiffs', and upheld the agency's decision. The district court rejected plaintiffs' contention that a health claim for a dietary supplement made in accordance with § 343(r)(5)(D) cannot be regulated by FDA as a drug claim because Congress clearly intended health claims to include any nutrient-disease claim, not just risk reduction claims.[9] Slip op. 9 (JA 2182). It concluded instead that claims about the effects of a dietary supplement on an existing disease do not fall within the scope of the health claim provisions in the statute. Slip op. 11-21 (JA 2184-94). The district court reached that conclusion after determining that the statute and the legislative history did not

[9] "Risk reduction" is shorthand for "reducing the risk of contracting a disease." AR 723 n.3 (JA 732).

provide a clear answer to the question (slip op. 11-17; JA 2184-90), but finding that the intertwined drug and dietary supplement definitions, as well as the legislative history, supported the reasonableness of FDA's interpretation (slip op. 17-21; JA 2190-94). The district court, therefore, concluded that FDA's interpretation did not violate the terms of the FDCA (ibid.) and that FDA's denial of plaintiffs' petition was not arbitrary under the APA (slip op. 19, 21-22; JA 2192, 2194-95). The court further determined that the denial did not violate plaintiffs' First Amendment commercial speech rights since the claim that plaintiffs wanted to make was contrary to law. Slip op. 22-24 (JA 2195-96).

Summary of Argument

The issue in this case is whether a claim to treat a disease can be made as a "health claim" under the NLEA, or whether health claims are properly limited to claims about the relationship of a nutrient to preventing or reducing the risk of a disease (such as "soy protein may reduce the risk of heart disease"). The agency's determination that the FDCA excludes treatment claims from the health claims provision is compelled by statute. The district court's decision, therefore, should be affirmed.

1. a. Plaintiffs argue that a single provision of the FDCA, § 343(r)(1)(B), requires FDA to authorize its proposed claim for the treatment of the symptoms of

BPH. In plaintiffs' view, this provision provides a complete "safe harbor" for dietary supplements from regulation as drugs. However, FDA concluded, and the district court agreed, that the statute as a whole, its purpose, and the legislative history compel a different result. The definitions of "dietary supplement" in § 321(ff) and "drug" in § 321(g)(1) make clear that dietary supplements are only partially excluded from the drug definition and, therefore, are properly regulated as drugs in appropriate circumstances. Indeed, Congress specifically rejected a definition of "dietary supplement" that would have completely excluded dietary supplements from the drug definition.

This partial "safe harbor" is available only for "prevention" claims that would otherwise fall within the drug definition, § 321(g)(1)(B), not "diagnosis," "cure," "treatment," or "mitigation" claims. Two specific statutory indicators make this clear. First, each and every one of the ten nutrient-disease relationships that Congress directed FDA to study for health claim purposes involves "prevention," but not "treatment" or the other elements of the drug definition. Second, the prevention/treatment distinction is the only line that preserves the statutory distinction between medical foods and ordinary foods.

In addition, an essential purpose of the FDCA is to make sure that drug products are proven safe and effective before they can be sold. Given this essential

purpose, a total exemption of dietary supplements from the drug provisions of the statute would have to be explicit and unambiguous. Congress, however, explicitly adopted only a partial exemption.

Moreover, the legislative history is consistent with, and in no way contradicts, FDA's understanding. The relevant statements in the legislative history speak of health claims in terms of "prevention" rather than "treatment" or the other elements of the drug definition. The legislative history further indicates that the common purpose behind all three main parts of the NLEA – the nutrition labeling, nutrient content claims, and health claim provisions – was to promote long-term health maintenance and prevention of disease by providing truthful, scientifically valid information to consumers on the food label.

b. Even if the statute were ambiguous, FDA's interpretation is reasonable and should be upheld. The reasonableness of FDA's action is demonstrated not only by the statutory and legislative history arguments already discussed, but also the fact that, at best, plaintiffs can only hypothesize a tension between § 343(r)(1)(B) and the definitions of "dietary supplement" and "drug." The dietary supplement and drug definitions directly undermine plaintiffs' basic thesis, however, and compel FDA's understanding of the statute: that dietary supplements are not completely exempt from drug regulation.

In addition, FDA's understanding of the statute is supported by critical public health concerns. FDA was concerned that manufacturers of foods and dietary supplements seeking to sell their products for disease treatment would avoid drug regulation by using the health claims process. This concern is based on the fact that a significant percentage of drugs currently prescribed by physicians are plant compounds or are related to plants. If health claims were permitted for disease treatment, foods and dietary supplements could avoid not only the preapproval and labeling requirements for drugs, but, equally importantly, the stringent post-approval reporting and other requirements, including adverse event reporting, that help to ensure continuing safety and efficacy after approval.

Further, as to saw palmetto in particular, FDA was concerned in its decision that, because prostate and bladder cancer present symptoms like BPH, self-medication could cause men to miss an early diagnosis of cancer with irreparable consequences. Moreover, as a general matter, it is important to regulate products intended to treat disease as drugs to ensure that they meet the high standards of safety and effectiveness appropriate to treat people with existing disease conditions. In this regard, in 1990, FDA had prohibited the marketing of saw palmetto as an over-the-counter drug because it was found not to be generally recognized as safe and effective for that use. FDA saw no congressional intent to permit dietary supplements to

circumvent these safety and efficacy concerns through the health claim provisions.

c. Finally, contrary to plaintiffs' contention, FDA's denial of plaintiffs' petition is entirely consistent with the health claim authorized for foods low in saturated fat and cholesterol. As FDA explained in its rulemaking, the authorized claim says that diets low in saturated fat and cholesterol reduce the risk of heart disease — a classic risk reduction claim. Although the claim also mentions that such diets lower cholesterol, the purpose of this reference is to explain the mechanism by which the risk of heart disease is reduced, not to make a claim for the treatment of elevated cholesterol levels. In contrast, plaintiffs want to make a claim, not about reducing the risk of developing BPH, but about treating the symptoms of BPH.

2. Plaintiffs' First Amendment claims are without merit. First, the key issue is whether a dietary supplement whose intended use is to treat disease must be regulated under the FDCA's drug provisions or whether its health claim provisions also apply. FDA has ruled that the drug provisions apply and therefore has not rendered a decision on the merits of plaintiffs' proposed claim under the health claim provisions. Therefore, at this point, plaintiffs have no claim that FDA violated the First Amendment vis-a-vis the health claim provisions. Second, given that the FDCA's drug provisions apply, if plaintiffs were to distribute saw palmetto in interstate commerce with the proposed claim, that claim could be considered as

evidence, along with any other relevant sources, of intended use as a drug. Such evidentiary use of speech does not violate the First Amendment. Third, the denial of plaintiffs' petition presents no First Amendment problem because the underlying transaction to which the claim relates — the proposed distribution of an unapproved new drug — would itself be unlawful. There is no First Amendment right to engage in speech about an unlawful activity.

Argument

Introduction.

For the reasons stated in Point I, infra, the statute compels FDA to treat claims about effects on an existing disease as falling within the scope of the FDCA's drug provisions, not its health claim provisions. For that reason, plaintiffs err in contending (Pl. Br. at 8-9) that the Court should address the constitutional argument first under the constitutional avoidance doctrine. See, e.g., United States v. Oakland Cannabis Buyers' Co-op, 532 U.S. 483, 494 (2001) ("The canon of constitutional avoidance has no application in the absence of statutory ambiguity."). Moreover, for the reasons stated in Point II, infra, plaintiffs' constitutional claims are without merit.[10]

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[10] Pearson v. Shalala, 164 F.3d 650, does not compel a different approach. In Pearson, the Court addressed the constitutional issue first but that was because, unlike here, there was no statutory issue about whether the proposed claims were within the

I. The FDCA Does Not Permit Dietary Supplement Health Claims To Encompass A Claim That The Supplement Treats An Existing Disease.

"Chevron, U.S.A., Inc. v. Natural Resources Defense Council, Inc., 467 U.S. 837 * * * (1984), governs review of agency interpretation of a statute which the agency administers." Bell Atlantic Telephone Companies v. FCC, 131 F.3d 1044, 1047 (D.C. Cir. 1997). Under the first step of Chevron, the reviewing court is required to "exhaust the 'traditional tools of statutory construction' to determine whether Congress has spoken to the precise question at issue." Ibid. The traditional tools in the search for plain meaning "include examination of the statute's text, legislative history, and structure * * * as well as its purpose * * *." Ibid. (citations omitted). If the search "yields a clear result," Congress has expressed its intention as to the question and deference does not come into play. Ibid. However, if the statute is silent or ambiguous with respect to the specific issue, then Congress has not spoken clearly, and the court will defer to the agency if its interpretation is permissible. Chevron, 467 U.S. at 843; Bell Atlantic, 131 F.3d at 1047.

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scope of the health claim provisions of the statute. It was uncontested that the health claim provisions applied, so the key issue was whether FDA's rejection of proposed claims, following a review pursuant to those provisions, was a First Amendment violation.

A. The Plain Meaning Of The FDCA Compels FDA's Interpretation.

1. The statute as a whole and its purpose compel FDA's interpretation.

a. As a general matter, a "drug claim" – a claim that an article can be used for "the diagnosis, cure, mitigation, treatment, or prevention of disease" – subjects the article to regulation as a drug under the FDCA. 21 U.S.C. 321(g)(1)(B). At the same time, a manufacturer of a dietary supplement may make a "health claim" — a claim that "characterizes the relationship of any nutrient * * * to a disease or a health-related condition" — without thereby subjecting the supplement to regulation as a drug. Id. § 343(r)(1)(B). The central issue in this case concerns the statutory relationship between "drug claims" on the one hand and "health claims" on the other. More specifically, the issue is whether the statutory definition of "health claim" was intended to reach claims that a dietary supplement can treat an existing disease, or whether the definition was directed instead at claims that a supplement can prevent or reduce the prospective risk of developing diseases.

Viewed in isolation, the text of 21 U.S.C. 343(r)(1)(B) does not specifically answer that question. The language of § 343(r)(1)(B) does not refer specifically to the treatment of diseases, nor does it otherwise elaborate on what kind of "relationship" between nutrients and diseases Congress had in mind when it enacted

the provision. The plaintiffs nonetheless argue that § 343(r)(1)(B) allows manufacturers of dietary supplements to make any claim that a drug can make — that it can be used to diagnose, cure, treat, mitigate, or prevent a disease or its symptoms, see § 321(g)(1)(B) — and yet be exempt from regulation as a drug. Pl. Br. at 22; Complaint ¶ 32 (JA 1661). See also Amicus Br. at 2-4. In other words, in plaintiffs' view, the general language of § 343(r)(1)(B) is a complete exemption for dietary supplements from regulation as drugs. Plaintiffs, however, have misstated the scope and meaning of this provision.

Section 343(r)(1)(B) merely describes the general structure of a health claim — i.e., a statement which posits the relationship between any nutrient and a disease. It does not state that dietary supplements are totally exempt from regulation as drugs. Indeed, it could not mean that because the definition of a "dietary supplement" in § 321(ff) makes clear that a dietary supplement is only partially excluded from the drug definition. A "dietary supplement," in pertinent part, is defined as "a product (other than tobacco) intended to supplement the diet that bears or contains * * * an herb or other botanical," and such product "shall be deemed to be a food" "[e]xcept for purposes of [the definition of 'drug' in § 321]." 21 U.S.C. 321(ff) (emphasis added). By definition, therefore, a dietary supplement can be both a food and a drug and, if the latter, regulated as such.

Similarly, the drug definition in 21 U.S.C. 321(g)(1)(B), in pertinent part, states that a "drug" is any "article[] intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease" except that a "food or dietary supplement" for which a health-related claim under §§ 343(r)(1)(B) and 343(r)(5)(D) is made "is not a drug solely because the label or the labeling contains such a claim." (Emphasis added.) The drug definition thus provides, as well, that dietary supplements in certain circumstances will fall within the scope of the drug definition and, accordingly, be regulated as drugs. See Pearson v. Shalala, 164 F.3d at 652. See also discussion, infra, at pp. 37-39. In short, the dietary supplement and drug definitions explicitly create only a partial exemption from drug regulation for dietary supplements. See FDA v. Brown & Williamson Tobacco Corp., 529 U.S. 120, 133 (2000) (it is "a fundamental canon of statutory construction that the words of a statute must be read in context and with a view to their place in the overall statutory scheme") (internal quotation marks and citation omitted); Bell Atlantic, 131 F.3d at 1047 (the "literal language of a provision taken out of context cannot provide conclusive proof of congressional intent, any more than a word can have meaning without context to illuminate its use").

Had Congress wanted to create a complete "safe harbor" (Pearson v. Shalala, 164 F.3d at 652) from drug regulation for dietary supplements, it would have

excepted the definition of "dietary supplement" from the drug definition entirely. In fact, however, Congress specifically refused to adopt the approach urged by plaintiffs because Congress specifically rejected a definition that would have completely excepted dietary supplements from the definition of a drug under the statute. See 140 Cong. Rec. S11706 (daily ed. Aug. 13 1994) (refusing to add a provision to DSHEA's drug definition that would have stated, subject to certain exceptions, that "[t]he term 'drug' does not include a dietary supplement as defined in paragraph (ff)"). See also United States v. Ten Cartons * * * Ener-B Vitamin B-12, 72 F.3d 285, 287 (2d. Cir. 1995) (product deemed dietary supplement under § 321(ff) can also be classified as a drug under § 321(g)(1) because Congress considered and rejected a definition that would have made the terms mutually exclusive); Nutrilab, Inc. v. Schweiker, 713 F.2d 335, 336 (7th Cir. 1983) ("well-established" that definitions of "food" and "drug" are not mutually exclusive). As a result, the definitions are not mutually exclusive. Therefore, contrary to plaintiffs' central thesis (Pl. Br. at 23), dietary supplements enjoy only a partial "safe harbor" from drug regulation.[11] Cf. INS v. Cardoza-Fonseca, 480 U.S. 421, 442-43 (1987) ("Few principles of statutory construction are

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[11] In Pearson v. Shalala, 164 F.3d at 652, this Court noted that "certain" dietary supplements are excepted from the drug definition if they bear an FDA-authorized health claim. The Court never stated, as plaintiffs suggest (Pl. Br. at 23), that dietary supplements are totally excepted from the drug definition.

more compelling than the proposition that Congress does not intend sub silentio to enact statutory language that it has earlier discarded in favor of other language.").[12]

The foregoing discussion, moreover, is entirely consistent with an "essential purpose" of the FDCA that "pervades" the statute, namely, that "[drug] products must be proven safe and effective before they can be sold * * *." Brown & Williamson, 529 U.S. at 133 (internal quotation marks and citation omitted). Given the central importance of drug regulation, any abrogation of such regulation and the extent of such abrogation would have to be explicit. Cf. Director of Revenue of Missouri v. CoBank ACB, 531 U.S. 316, 324 (2001) (Court refused to read amendments to statute as having "made a radical – but entirely implicit – change" in the law sub silentio). But, here, the dietary supplement and drug definitions are clear, and both explicitly create only a partial exemption of dietary supplements from drug regulation. There is absolutely nothing in the NLEA to indicate that Congress intended to abrogate entirely the safety and efficacy requirements (see 21 U.S.C. 355) for articles that

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[12] Plaintiffs contend that Congress specifically rejected FDA's proposed "health messages" definition. See, e.g., Pl. Br. at 19, 20, 25-26 & n.43. Plaintiffs' argument is based on a comparison of FDA's 1990 proposed rule with the language Congress adopted in § 343(r)(1)(B). Pl. Br. at 26. In fact, however, Congress did not first propose FDA's "health messages" rule and then specifically reject it by employing contrary language. Even if Congress had rejected FDA's proposed "health messages" rule, that would not help plaintiffs' cause. The fact still remains that, under the unambiguous language of the statute, dietary supplements are only partially excluded from the drug definition.

claim to treat disease or the symptoms of disease merely because they also meet the definition of food or dietary supplement. The partial exemption of dietary supplements from drug regulation undercuts plaintiffs' contention that Congress created a parallel universe of foods and dietary supplements completely free from drug regulations. Compare 21 U.S.C. 321(g)(1)(C) (complete exemption of foods from "structure/function" component of drug regulation) with 21 U.S.C. 321(g)(1)(B) (no such exemption for "disease" component of definition). There is therefore no merit to plaintiffs' contention that the only limitations on the marketing of dietary supplements are those imposed by the FDCA's dietary supplement and health claim provisions. Pl. Br. at 27-30, citing 21 U.S.C. 321(ff), 342(f)(1), 343(r)(1)(B), 350b.

b. Both the dietary supplement and drug definitions establish that the exemption for dietary supplements is only partial, but they do not define the extent of the exemption. The bounds of the exemption are reflected elsewhere in the statute. Two other statutory provisions demonstrate that the exemption was meant to extend only to "prevention" claims, not "treatment" claims (or "diagnosis," "cure, or "mitigation" claims).[13]

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[13] Hereinafter, we will use "treatment" as a synonym for "treatment," "mitigation," and "cure" because "claims to treat, mitigate, and cure disease are closely related, in that all are claims to have an effect on an existing disease." AR 722-723 (JA 731-32). Since "diagnosis" does not involve an effect on an existing disease and is not at issue here in any way, we will no longer refer to it specifically.

First, Congress directed the agency to consider whether ten specific "nutrient-disease" relationships qualified as "health claims" under the Act. See Pub. L. No. 101-535, §§ 3(b)(1)(A)(vi) & (x), 104 Stat. 2361 (21 U.S.C. 343 note). These relationships — calcium and osteoporosis; dietary fiber and cancer; lipids and cardiovascular disease; lipids and cancer; sodium and hypertension; dietary fiber and cardiovascular disease; folic acid and neural tube defects; antioxidant vitamins and cancer; zinc and immune function in the elderly; and omega-3 fatty acids and heart disease — all involve the potential long-term prevention of a disease, 55 Fed. Reg. at 5192 (col. 1), which includes the reduction of risk of developing a disease or other health-related condition relating to dietary practices. None involves treatment of disease. The ten relationships demonstrate exactly what Congress had in mind when it added § 343(r)(1)(B) to the law in 1990 — i.e., that the nutrient-disease relationships referred to in § 343(r)(1)(B) were limited to "prevention" relationships and that, accordingly, the "safe harbor" would extend only that far.[14] Cf. United

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[14] Six of the relationships were ones proposed by FDA prior to enactment of the NLEA and were based on FDA's long-held view of the difference between disease treatment and risk reduction. See 55 Fed. Reg. at 5184 (cols. 2-3). Congress's addition of four relationships consistent with the six previously published by FDA, therefore, also serves as endorsement of FDA's distinction between prevention and treatment. Cf. Lorillard v. Pons, 434 U.S. 575, 580 (1978) ("Congress is presumed to be aware of an administrative or judicial interpretation statute and to adopt that interpretation when it re-enacts a statute without change.").

States v. An Article of Drug * * * Bacto-Unidisk, 394 U.S. 784, 799-800 (1969) (difference between "drug" and "device" under FDCA determined by reference to statements in legislative history characterizing what a device is).

Second, that the "safe harbor" is limited to "prevention" claims is also compelled by the distinction that the FDCA makes between medical foods and ordinary (non-medical) foods. In 1988, two years before enactment of the NLEA, Congress defined a medical food in relevant part as a food taken "enterally under the supervision of a physician and which is intended for the specific dietary management of a[n] [existing] disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation." 21 U.S.C. 360ee(b)(3) (emphasis added). Medical foods, in other words, are foods intended to treat or manage a disease that an individual already has.

In the NLEA, two years later, Congress permitted foods to make health-related claims, see 21 U.S.C. 343(r)(1)(B), but medical foods were specifically exempted from the health claim provisions, see 21 U.S.C. 343(r)(5)(A). See also House Report at 22 (noting the exemption). In exempting medical foods from the health claim provisions, Congress created a distinction between medical foods and other foods with the result that health claims for ordinary foods would focus on disease differently from medical foods. Whereas medical foods target existing diseases or

conditions, health claims for ordinary foods (which include dietary supplements) would be targeted at diseases or conditions that people have not yet contracted — i.e., to "prevent" diseases or conditions, rather than treat them. If ordinary foods could make "treatment" claims, that would severely blur the distinction between the two in contravention of the language and structure of the statute. See AR 727 (JA 736) (Congress created "separate regulatory spheres" for medical foods and ordinary foods).

Plaintiffs contend that the distinction between treatment and prevention fails because there is "substantial overlap" in the two concepts. See Pl. Br. at 33. There is no overlap. The purpose of prevention, including risk reduction, is to try to ensure that the disease does not occur, rather than treat or mitigate the signs and symptoms or the underlying cause of an existing disease.

The amicus argues that support for plaintiffs' position comes from the drug definition, § 321(g)(1) — a "food or dietary supplement" for which a health-related claim under §§ 343(r)(1)(B) and 343(r)(5)(D) is made "is not a drug solely because the label or the labeling contains such a claim." Amicus Br. at 8. In the amicus's view, the drug definition does not allow "FDA to narrow the health claims definition" (ibid.), and the fact that the definition uses the term "solely" means only "that use of an authorized health claim does not preclude the FDA from finding that other claims

made for the same dietary supplement product are drug claims." Amicus Br. at 8 (emphasis in original). The amicus then gives this example: "use of an authorized health claim on the label of a dietary supplement (e.g., folate reduces the risk of neural tube defects) does not give a manufacturer blanket immunity to include other claims for the product that would otherwise be classified as drug claims (e.g., folate cures cancer)." Ibid. This argument, however, reinforces FDA's point: the safe harbor extends only to the "prevention" element of the drug definition and not to the definition's other elements.

The use of the term "solely" in the drug definition, moreover, clearly demonstrates that Congress contemplated that, in certain circumstances, dietary supplements could bear an authorized health claim and, also, could be regulated as drugs based on other evidence of intended use to treat a disease.[15] In fact, the

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[15] It has long been established that the touchstone for deciding whether a product is a "drug" is the product's intended use. See 21 U.S.C. 321(g)(1). See also Action on Smoking and Health v. Harris, 655 F.2d 236, 238 (D.C. Cir. 1980). Intended use may be determined from any relevant source, including product labeling, advertising, promotional material, and oral or written representations by the vendor. See 21 C.F.R. 201.128; Action on Smoking and Health v. Harris, 655 F.2d at 238; United States v. Storage Spaces Designated Nos. "8" and "49", 777 F.2d 1363, 1366 (9th Cir. 1985); United States v. An Article of Device * * *. Toftness Radiation Detector, 731 F.2d 1253, 1256-57 (7th Cir. 1984); United States v. An Article * * * Consisting of 216 Bottles, More or Less, * * * Sudden Change, 409 F.2d 734, 739 (2d Cir. 1969); United States v. Article of Drug Designated B-Complex Cholinos, 362 F.2d 923, 925-26 (3d Cir. 1966).

amicus's concession (see above) that "drug claims" are not completely "immuni[zed]" under § 343(r)(1)(B) makes this precise point. Amicus Br. at 8. See also AR 1210 (JA __) (statement by Traco Labs, Inc. similar to the amicus's). All FDA has done is follow Congress's lead with respect to the ten nutrient-disease relationships and the medical foods/ordinary foods dichotomy to make the determination that an intended use for "prevention" falls within the scope of a health claim (and thus the "safe harbor") but an intended use for "treatment" does not.[16]

2. The Legislative History Also Compels FDA's Interpretation.

Where a statute has a plain meaning, resort to legislative history is unnecessary. See, e.g., United States v. Gonzales, 520 U.S. 1, 6 (1997) ("Given the straightforward statutory command, there is no reason to resort to legislative history."). Only if a plain meaning analysis would produce "absurd" results or results antithetical to the intention of Congress is resort to legislative history appropriate. Inter-Modal Rail Employees Ass'n v. Atchison, T&SF Ry. Co., 520 U.S. 510, 516 (1997). Even if the legislative history merely supported (as opposed to compelled) FDA's understanding of the statute, it does not produce results antithetical to Congress's intent. Indeed,

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[16] That the term "solely" in the drug definition indicates an overlap in the drug and health claim provisions does not help plaintiffs' cause because it does not shed any light on what an authorized health claim is in the first place, only that an authorized health claim under § 343(r), in and of itself, does not make the product bearing such a claim a drug.

here the legislative history of the NLEA strongly supports FDA's position.

The legislative history of the NLEA consistently characterized health claims as claims about reducing the risk of developing a disease or helping to prevent a chronic disease, not treatment. For example, the House Report stated that "[t]he bill provides a process for the orderly regulation of disease claims (such as 'fiber prevents cancer')." House Rep. at 8 (AR 736) (JA 745). The Report noted that "[t]he Surgeon General has advised Americans that diets low in fats, low in salt and high in fiber can reduce the risk of chronic diseases such as cancer and heart disease. Health claims supported by significant scientific agreement can reinforce the Surgeon General recommendations and help Americans to maintain a balanced and healthful diet." House Rep. at 9-10 (AR 738) (ja 747). And, in referring to § 343(r)(3), the Report stated that that section "regulates disease claims" and "prohibits any disease claim (for example, 'fiber helps to prevent cancer') unless the claim meets the requirements of regulations promulgated by the Secretary." House Rep. at 20 (AR 749) (JA 758). See also 136 Cong. Rec. H5841 (statement of intent of changes since bill was reported out of committee) ("fiber prevents cancer") (AR 760) (JA 769; col. 3).

Numerous statements of individual Members of Congress and Senators evidence the same intent. See 136 Cong. Rec. H5841 (statement of Rep. Waxman) ("bran prevents cancer") (AR 760) (JA 769); 136 Cong. Rec. S16,609 (Statement of

Sen. Mitchell) ("reduces the risk of cancer") (AR 768) (JA 777); 136 Cong. Rec. H12,953 (statement of House floor managers) ("fiber in cereal prevents cancer") (AR 775) (JA 784); 136 Cong. Rec. H12,954 (statement of Rep. Madigan) ("bran prevents cancer") (AR 776) (JA 785).

The legislative history further indicates that the common purpose behind all three main parts of the NLEA – the nutrition labeling, nutrient content claims, and health claim provisions – was to promote long-term health maintenance and prevention of disease by providing truthful, scientifically valid information to consumers on the food label. See 136 Cong. Rec. H5843 (statement of Rep. Moakley) (legislation responds to Americans' increasing concern about their diets and reducing the risk of disease) (AR 762) (JA 771); 136 Cong. Rec. H5843 (statement of Rep. Madigan) (question under consideration is how to most effectively inform consumers about health risks related to diet) (AR 762) (JA 771); 136 Cong. Rec. S16,609 (statement of Sen. Metzenbaum) (many Americans use dietary supplements to help prevent chronic disease; rapid scientific advances link nutritional substances to maintenance of long-term health and prevention of long-term disease) (AR 768) (JA 777); 136 Cong. Rec. S16,610-11 (statement of Sen. Hatch) (vitamins and minerals are important in helping to prevent certain serious illnesses and health problems; because of rapid scientific advances linking the prevention of long-term

disease to improved nutritional supplementation, important to allow dietary supplements to be marketed so that consumers are informed of the health or disease-prevention benefits they may confer) (AR 769-70) (JA 778-79); 136 Cong. Rec. H12,954 (statement of Rep. Moakley) (healthy eating can lower risk for certain illnesses, such as heart disease and cancer) (AR 776) (JA 785).

Moreover, the foregoing statements were made against the backdrop of FDA's prior rulemaking. The preamble to the 1987 proposed rule stated that health claims "should not imply that a particular food be used as part of a drug-like treatment or therapy oriented approach to health care." 52 Fed. Reg. at 28845 (col. 3). The 1990 proposal would have explicitly limited acceptable health claims to claims about "the value that ingestion (or reduced ingestion) of a dietary component may have in either lowering the risk, or forestalling the premature onset, of a particular chronic disease condition." 55 Fed. Reg. at 5192 (col. 1). Both proposed rules, as well as the scientific publications cited to support them — the National Research Council's 1989 report entitled "Diet and Health: Implications for Reducing Chronic Disease Risk" (AR 779 Attachment A) and the 1988 Surgeon General's Report on Nutrition and Health (AR 781 Attachment B) — focused on diet as a means of reducing the risk of developing chronic diseases, such as cancer and coronary heart disease. Hence, before the passage of NLEA, health claims had a defined meaning, understood by

representatives of industry as well as consumer groups as focused on maintaining good health (or avoiding poor health), and not on treating an existing disease. See AR 1462-87; 1489-94; 1496-1534 (JA 1472-97, 1499-1504, 1506-1544). Cf. Mead Johnson Pharmaceutical Group v. Bowen, 838 F.2d 1332, 1336 (D.C. Cir. 1988) (although a term in the 1984 Hatch-Waxman amendments to the FDCA was not expressly defined in the Amendments, "it had, at the time the Hatch-Waxman Amendments were enacted, a precise and undisputed meaning" given to it by FDA, and the court "found absolutely no reason to believe that Congress intended the term * * * to mean anything other than what the FDA understood it to mean").

Plaintiffs argue that none of these statements proves FDA's point because, while the statements speak of health claims in terms of risk reduction, Congress did not explicitly state that health claims could not speak in terms of disease treatment. Pl. Br. at 19 & n.37, 24. To the contrary, the statements clearly support FDA's position in this case. In contrast, nothing in these statements supports, much less compels, plaintiffs' interpretation.[17]

Further, it is significant that FDA's construction of the health claims provision was published before Congress enacted the DSHEA and was not modified by that

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[17] In any event, there is no merit to plaintiffs' argument because it makes the illogical assertion that, because Congress said "X" and did not say "not Y," that "Y" is clear and "X" is not or, alternatively, that "Y" is a stronger proposition than "X."

statute. In its 1994 final rule, FDA stated unequivocally that claims "to correct an abnormal physiological function caused by a disease or health-related condition" would be drug claims rather than health claims. 59 Fed. Reg. at 407 (col. 2). FDA also advised that "statements that a product may be effective in the cure, mitigation, treatment or prevention of disease will make the product a drug," but that "statements that a product may reduce the risk of developing a disease or health-related condition [might] or [might] not make the product a drug." 59 Fed. Reg. at 412 (col. 3).

When Congress enacted the DSHEA later in 1994, Congress further defined dietary supplements and clarified the types of claims that could be made for supplements under the Act, see 21 U.S.C. 321(ff) and 343(r)(6), but did not amend the health claim provisions of § 343(r) or exempt dietary supplements completely from the drug definition. Indeed, as previously stated, Congress did the opposite and rejected a provision that would have made the "drug" and "dietary supplement" definitions mutually exclusive. See pp. 31-32, supra. Thus, Congress's actions support, if not compel, FDA's understanding that, when a dietary supplement makes a claim about treatment of disease, it is making a drug claim and should be regulated as a drug. See Brown & Williamson, 529 U.S. at 133 ("[t]he meaning of one statute may be affected by other Acts, particularly where Congress has spoken subsequently and more specifically to the topic at hand"); Lorillard v. Pons, 434 U.S. at 580

("Congress is presumed to be aware of an administrative or judicial interpretation statute and to adopt that interpretation when it re-enacts a statute without change.").

Plaintiffs assert that post-enactment legislative history of the DSHEA, S. Rep. No. 103-410 (Oct. 8, 1994), supports their interpretation. See Pl. Br. at 25 n.42. The assertion is wrong for many reasons. First, as plaintiffs acknowledge (ibid.), Congress took the unusual step of specifically excluding the report from consideration as legislative history. See 140 Cong. Rec. S14801 (Oct. 7, 1994), reprinted in 1994 U.S.C.C.A.N. 3523. See also slip op. 16 (JA 2189). Second, statements made by subsequent legislatures in the form of reports and floor statements — rather than actual legislation — about prior legislation are at best "legislative dicta." Dunn v. Commodity Futures Trading Comm'n, 519 U.S. 465, 479 (1997). Third, even if the report had value, the cited examples of potential benefits of herbs and amino acids were included in a discussion of the need for legislation generally and were not used in any discussion of the provisions of the DSHEA or the NLEA. In context, therefore, they provide no insight into how Congress in 1994 interpreted the NLEA's health claims provisions.

Although the district court believed there was some ambiguity in the DSHEA's legislative history, it acknowledged that Congress specifically stated that the DSHEA amendments were added to recognize "the benefits of dietary supplements to health

promotion and disease prevention." Slip op. 16 (JA 2189), quoting Pub. L. No. 103-417, 108 Stat. 4325 at § 2(2) (emphasis in opinion). This statement is fully consistent with the House Report accompanying the NLEA, the individual statements of congressmen and senators previously discussed, and the ten nutrient-disease relationships that Congress directed FDA to study. Disease "prevention" is precisely the element in the drug definition where FDA understood Congress to have established the overlap in the drug and health claim provisions of the statute and thus created the potential "safe harbor" for dietary supplements. The DSHEA therefore ratifies FDA's understanding that health claims are limited to claims about disease prevention.

B. Even If The FDCA Were Ambiguous, FDA's Interpretation Is Permissible and Therefore Must Be Upheld.

In United States v. Mead Corp., 533 U.S. 218 (2001), the Supreme Court held that "administrative implementation of a particular statutory provision qualifies for Chevron deference when it appears that Congress delegated authority to the agency generally to make rules carrying the force of law," that "the agency interpretation claiming deference was promulgated in the exercise of that authority," and that "[d]elegation of such authority may be shown * * * by an agency's power to engage in adjudication or notice-and-comment rulemaking." 533 U.S. at 226-227. See also

Aid Ass'n for Lutherans v. United States Postal Service, 321 F.3d 1166, 1174 (D.C. Cir. 2003), citing Chevron, 467 U.S. at 843-44, and United States v. Mead Corp., 533 U.S. at 226-27. Assuming ambiguity in the statute, FDA's interpretation is reasonable and entitled to deference because FDA's decision was rendered pursuant to express authority under 21 U.S.C. 343(r) to adjudicate health claim petitions, and FDA's decisions on such petitions have the force of law. Moreover, FDA's interpretation is entitled to deference because it was the result of a rulemaking-like proceeding. The public had opportunity to comment on plaintiffs' petition and the statutory issue presented, AR 721-22 (JA 730-31), and the agency considered those comments in its decision. Id. at 724 (JA 733). Furthermore, FDA is entitled to deference because its interpretation is one of longstanding which it has consistently stated in notice and comment rulemaking. Id. at 727-728 (JA 736-37). See Barnhart v. Walton, 122 S. Ct. 1265, 1270 (2002) (deferring to agency's interpretation embodied in regulations because "regulations reflect the Agency's own longstanding interpretation" embodied in agency manuals, rulings and ruling letters).

In Point I(A), we demonstrated that the statute as a whole, its structure, and the legislative history compel FDA's decision. These same arguments also apply to demonstrate why FDA's decision was reasonable and permissible under Chevron step two. Accordingly, we add only the following arguments in support of the

reasonableness of FDA's action.

1. Nothing in the language of the statute as a whole or the legislative history supports plaintiffs' interpretation that dietary supplements are completely exempt from regulation as drugs. At best, plaintiffs can only hypothesize a tension (a tension that we believe is not present) between what plaintiffs argue is the broad language in § 343(r)(1)(B), which speaks of health claims in general terms as "the relationship of any nutrient * * * to a disease or health-related condition," and the definitions of "dietary supplement" (§ 321(ff)) and "drug" (§ 321(g)(1)(B)), which clearly state that in certain circumstances a dietary supplement can be a drug. Since the latter provisions undermine the central premise of plaintiffs' argument, namely, that the health claim provisions completely exempt dietary supplements from drug regulation, plaintiffs' interpretation also falls since it is based on that premise.

2. In addition to the statute, its structure, and the legislative history, FDA's interpretation of the FDCA is supported by critical public health concerns. As the agency found, approximately 94% of prescription drugs, and almost all over-the-counter drugs for disease uses, are for treatment rather than prevention of disease. AR 730, 925-1023 (JA 739, 934-1032). Because Congress evidenced no intent to dismantle the drug regulatory scheme, and because Congress evidenced its intent that health claims be in the nature of prevention (or risk reduction), the agency determined

that the statutory "safe harbor" would be limited to "prevention" claims rather than the more encompassing "treatment" category. See United States v. An Article of Drug * * * Bacto-Unidisk, 394 U.S. at 799 (in defining the distinction between drugs and devices under the FDCA, "the natural way to draw the line is in light of the statutory purpose") (internal quotations and citation omitted).

FDA was also concerned that manufacturers would seek to avoid drug regulation by using the health claims process instead. AR 730 (JA 739). As FDA has pointed out, about 25% of drugs currently prescribed by physicians are plant compounds and an additional 25% are related to plants. 59 Fed. Reg. at 413 (col. 1). Such commonly used drugs as digitalis, aspirin, quinidine, atropine, and hundreds of others were once considered herbals. Ibid. Many botanicals and other substances that are or could be marketed as dietary supplements have potential uses in treating disease. Under plaintiffs' view, such claims as "St. John's wort may cure depression" or "chromium may treat diabetes" could be made as "health claims." Such products would thereby avoid not only the preapproval and labeling requirements for drugs, but, equally importantly, the stringent post-approval reporting and other requirements, including adverse event reporting, that help to ensure continuing safety and efficacy after approval. See 21 U.S.C. 355(e) (authority to withdraw approval); § 355(k) (records and reports).

Plaintiffs argue that there is no merit to this "end-run" argument because the "serious adverse effects" associated with pharmacologically active substances would make them ineligible for dietary supplement status. Pl. Br. at 27-30. The point, however, is that FDA lacks authority to require premarket approval of dietary supplements.[18] Thus, if these products could not be regulated as drugs, FDA would have to rely on postmarket enforcement actions under the dietary supplement adulteration provisions in § 342(f), a less than adequate remedy in light of the fact that Congress requires premarket approval of drugs because of the serious public health risks at stake. See Pharmanex v. Shalala, 221 F.3d 1151, 1159 (10th Cir. 2000) (ruling that regulation of dietary supplement under § 342(f) does "not adequately respond[] to the FDA's strenuous objection that these provisions only empower the FDA to remove unsafe products rather than preclude their entry into the marketplace ab initio").

Further, the agency had found that it is important to regulate products intended to treat disease as drugs to ensure that they meet the high standards of safety and effectiveness appropriate for the care of sick people. AR 729-730 (JA 738-39). In this regard, as to saw palmetto in particular, in 1990, FDA had prohibited the

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[18] Certain new dietary ingredients require premarket review, but not premarket approval.

marketing of saw palmetto as an over-the-counter drug for BPH because it was found not to be generally recognized as safe and effective for that use. See, e.g., AR 729 (JA 738). Plaintiffs are now attempting to circumvent that decision and avoid drug regulation altogether by seeking authorization under the health claim provisions to market saw palmetto for exactly the same use, as a treatment for the symptoms of BPH. See AR 1, 22, 729-730 (JA 9, 30, 738-39).

Finally, plaintiffs contend that the statute should not be read to require regulation of their proposed claim under the drug provisions of the FDCA because the cost is prohibitive. Pl. Br. at 17-18 & n.35. This argument, of course, can have no bearing on whether the plain language of the statute compels regulation under the drug provisions. Even if there were some ambiguity in what the statute commanded, the Supreme Court has made clear that, where a public health statute is at issue, there must be a clear textual commitment to consider costs before a court can take that element into account in its analysis. Whitman v. American Trucking Ass'ns, 531 U.S. 457, 468 (2001). There is no such textual commitment here.[19]

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[19] In any event, plaintiffs incorrectly contend that submission of a new drug application is the only available avenue open to them under the Act's drug provisions. Pl. Br. at 17-18. The 1990 rule on saw palmetto made clear that any party can petition the agency to reconsider the decision that the product is a new drug and establish an over-the-counter monograph permitting interstate distribution (a much less expensive proposition than the new drug approval process). 55 Fed. Reg. at 6929 (col. 3); 21 C.F.R. 330.10(a)(12) (2000).

C. FDA's Determination Here Is Not Inconsistent With Other Health Claims That It Has Authorized.

Plaintiffs contend that FDA's decision violates the APA because it is inconsistent with the health claim authorized in 21 C.F.R. 101.75(e)(3) (2002): "A healthful diet low in saturated fat, total fat, and cholesterol * * * may lower blood cholesterol levels and may reduce the risk of heart disease * * *." Pl. Br. at 32. In plaintiffs' view, this claim makes the same kind of statement as their proposed claim for saw palmetto because the former concerns the treatment of high cholesterol, which plaintiffs say is a symptom of "heart disease." Pl. Br. at 33 (citing FDA's rulemaking pertaining to the distinction between "structure/function" and "disease" claims under 21 U.S.C. 343(r)(6), see 65 Fed. Reg. at 1018-19, but not FDA's original rulemaking which authorized the health claim, see 58 Fed. Reg. 2552, 2573(1993) and 58 Fed. Reg. 2739, 2757 (1993)).

FDA's rulemaking, however, makes clear that, although the claim mentions that diets low in saturated fat, total fat, and cholesterol may lower blood cholesterol levels, the purpose of this reference to lowering cholesterol levels is to explain the mechanism by which the risk of heart disease is reduced, not to make a disease treatment claim about hypercholesteremia or heart disease or the symptoms of either. See 58 Fed. Reg. at 2573 (cols. 1-2) (claim for fiber-containing fruits, vegetables, and

grains, and coronary heart disease found in 21 C.F.R. 101.77) (this reference is "reflective of the scientific evidence which links these dietary factors to heart disease risk via the intermediate mechanism of reducing blood LDL-cholesterol levels"). See also 58 Fed. Reg. at 2739-2757 (authorizing health claim for foods low in saturated fat and cholesterol and coronary heart disease found in 21 C.F.R. 101.75). The authorized claim therefore pertains to reducing the risk of heart disease and not to treating elevated cholesterol levels. Plaintiffs, in contrast, want to make a claim about the effects of saw palmetto, not as a mechanism for the prevention of BPH or reducing the risk of contracting BPH, but to directly treat the symptoms of BPH. Accordingly, there is no inconsistency between the authorized cholesterol/heart disease claim and FDA's determination here. See also slip op. 19 (JA 2192).[20]

II. There Is No First Amendment Violation.

Plaintiffs' First Amendment claims are without merit. First, the key issue is whether a dietary supplement whose intended use is to treat disease must be regulated under the FDCA's drug provisions or whether its health claim provisions also apply. FDA has ruled that the drug provisions apply and therefore has not rendered a

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[20] Plaintiffs refer on several occasions to claims that saw palmetto "supports prostate health" on currently marketed saw palmetto products. Pl. Br. at 4 & n.10, 16. As plaintiffs acknowledge (Pl. Br. at 4 n.10), this statement is a classic non-disease "structure/function" claim that can be made without prior authorization from FDA pursuant to 21 U.S.C. 343(r)(6).

decision on the merits of plaintiffs' proposed claim under the health claim provisions. Therefore, at this point, plaintiffs have no claim that FDA violated the First Amendment vis-a-vis the health claim provisions. If, however, this Court rules that plaintiffs' proposed claim must be reviewed under the health claim provisions of the FDCA (rather than regulated exclusively under the drug provisions as FDA held), a remand to FDA would be necessary to permit FDA to determine in further proceedings under the health claim provisions whether on the merits the proposed claim meets the "significant scientific agreement" standard in FDA's regulations, 21 C.F.R. 101.14(c)), and, if not, whether the claim could be rendered non-misleading with an appropriate disclaimer. Whether plaintiffs would have a First Amendment challenge to an FDA decision under the health claim provisions would depend on whether FDA authorizes the claim, permits the claim with a disclaimer, or rejects the claim outright. See Pearson v. Shalala, 164 F.3d 650 (Court considered First Amendment challenge to FDA's rejection of proposed health claims but only after FDA had reviewed the claims under the health claim provisions and rejected them).

Second, because plaintiffs' proposed claim is not a health claim, the primary statutory prohibition on plaintiffs' ability to legally market saw palmetto with the proposed claim is 21 U.S.C. 355, which prohibits the introduction into interstate commerce of any unapproved new drugs. See 21 U.S.C. 331(d) (prohibited act). As

previously discussed, FDA determined in 1990 that saw palmetto intended for use in the treatment of BPH was an unapproved new drug, and that its distribution in interstate commerce would accordingly violate the statute. Plaintiffs have not challenged that determination, nor have they submitted an application for approval of a new drug or a citizen's petition seeking reconsideration of FDA's 1990 rule, or otherwise sought approval to market saw palmetto as a drug.

Accordingly, were plaintiffs to distribute saw palmetto in interstate commerce with the proposed claim, that claim could be considered as evidence, along with any other relevant source, of intended use as a drug. See, e.g., Action on Smoking and Health, 655 F.2d at 238-39 ("[I]it is well established 'that the "intended use" of a product, within the meaning of the [FDCA], is determined from its label, accompanying labeling, promotional claims, advertising, and any other relevant source'"); and see n.15, supra. Such evidentiary use of speech does not violate the First Amendment. See Wisconsin v. Mitchell, 508 U.S. 476, 489 (1993) ("[t]he First Amendment * * * does not prohibit the evidentiary use of speech * * * to prove motive or intent"). The speech of a manufacturer has consistently been used to demonstrate the intended use of a product under the FDCA. See, e.g., United States v. Writers & Research, Inc., 113 F.3d 8, 11 (2d Cir. 1997) (product promoted as treatment or cure for cancer, AIDS, or other diseases is a "drug" under the FDCA,

regardless of whether it is "homeopathic"); Nutrilab, Inc. v. Schweiker, 713 F.2d at 336.

Third, the denial of plaintiffs' petition presents no First Amendment problem because the underlying transaction to which the claim relates — the proposed distribution of an unapproved new drug — would itself be unlawful. See slip op. 22-24 (JA 2195-97). The Supreme Court has made clear that speech concerning unlawful activity receives no First Amendment protection. See 44 Liquormart, Inc. v. Rhode Island, 517 U.S. 484, 497 n.7 (1996) (plurality opinion) ("the First Amendment does not protect commercial speech about unlawful activities"); Florida Bar v. Went For It, Inc., 515 U.S. 618, 623-24 (1995) ("the government may freely regulate commercial speech that concerns unlawful activity"); Zauderer v. Office of Disciplinary Counsel of Supreme Court of Ohio, 471 U.S. 626, 638 (1985) ("the States and the Federal Government are free to prevent the dissemination of commercial speech * * * that proposes an illegal transaction"); Central Hudson Gas & Elec. Corp. v. Public Serv. Comm'n of New York, 447 U.S. 557, 563-64 (1980) ("the government may ban * * * commercial speech related to illegal activity").

Pittsburgh Press Co. v. Pittsburgh Comm'n on Human Relations, 413 U.S. 376 (1973), is instructive. That case concerned a municipal ordinance that prohibited a newspaper from carrying a gender-based advertising column for certain positions of

employment. The ordinance also prohibited employers from engaging in gender discrimination with respect to those positions and from publishing, or causing to be published, any advertisement that indicated gender discrimination. Id. at 378, 388-89. The Court recognized that the advertisements at issue "signaled that the advertisers were likely to show an illegal sex preference in their hiring decision." Id. at 389. The Court held that any First Amendment interest in advertising a commercial transaction is "altogether absent when the commercial activity itself is illegal and the restriction on advertising is incidental to a valid limitation on economic activity." Ibid.; see also Central Hudson, 447 U.S. at 563-64.

The same analysis governs here. Pittsburgh Press involved unlawful conduct (unlawful gender discrimination) and this case involves potential unlawful conduct (the potential unlawful distribution of unapproved new drugs). In both cases, the commercial speech at issue (the advertisements in Pittsburgh Press and the proposed claim in this case) provides persuasive evidence of the intent or motive that is an element of the unlawful conduct. And here, as in Pittsburgh Press, "the restriction on advertising is incidental to a valid limitation on economic activity." Ibid.

In short, there can be no question that the FDCA's longstanding use of manufacturers' speech to determine the "intended" uses of their products is consistent with the Constitution. Because that traditional feature of the FDCA passes

constitutional muster, the denial of plaintiffs' petition also withstands scrutiny. See slip op. 22-24 (JA 2195-97).[21]

Conclusion

For the foregoing reasons, the district court's judgment should be affirmed.

Respectfully submitted,

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[21] Accordingly, plaintiffs' argument that the information which it wishes to place on its label is truthful scientific information (Pl. Br. at 11-15 & 14-15 n.31) is irrelevant.

D.C. CIRCUIT RULE 28(d) CERTIFICATE

This brief has been produced using proportional 14 point type in the "Times New Roman" style. I hereby certify that this brief complies with the word limitation set forth in Rule 32(a)(7)(B), Fed. R. App. P. According to the word counting feature of the Corel Word Perfect 7 Software used by the Department of Justice, this brief does not exceed 14,000 words; it contains 13,993 words (from and including the caption on page 1 through the signature block on page 58).

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I hereby certify that on this 25th day of June, 2003, I caused the foregoing Brief of the Federal Appellees to be served upon the Court and counsel by causing an original and 15 copies to be delivered via **HAND DELIVERY** to:

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STATUTORY AND REGULATORY ADDENDUM

§ 321. Definitions; generally

For the purposes of this chapter—

(a)(1) The term "State", except as used in the last sentence of section 372(a) of this title, means any State or Territory of the United States, the District of Columbia, and the Commonwealth of Puerto Rico.

(2) The term "Territory" means any Territory or possession of the United States, including the District of Columbia, and excluding the Commonwealth of Puerto Rico and the Canal Zone.

(b) The term "interstate commerce" means (1) commerce between any State or Territory and any place outside thereof, and (2) commerce within the District of Columbia or within any other Territory not organized with a legislative body.

(c) The term "Department" means the Department of Health and Human Services.

(d) The term "Secretary" means the Secretary of Health and Human Services.

(e) The term "person" includes individual, partnership, corporation, and association.

(f) The term "food" means (1) articles used for food or drink for man or other animals, (2) chewing gum, and (3) articles used for components of any such article.

(g)(1) The term "drug" means (A) articles recognized in the official United States Pharmacopoeia, official Homeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any article specified in clauses (A), (B), or (C) of this paragraph. A food or dietary supplement for which a claim, subject to sections 343(r)(1)(B) and 343(r)(3) of this title or sections 343(r)(1)(B) and 343(r)(5)(D) of this title, is made in accordance with the requirements of section 343(r) of this title is not a drug solely because the label or the labeling contains such a claim. A food, dietary ingredient, or dietary supplement for which a truthful and not misleading statement is made in accordance with section 343(r)(6) of this title is not a drug under clause (C) solely because the label or the labeling contains such a statement.

(2) The term "counterfeit drug" means a drug which, or the container or labeling of which, without authorization, bears the trademark, trade name, or other identifying mark, imprint, or device, or any likeness thereof, of a drug manufacturer, processor, packer, or distributor other than the person or persons who in fact manufactured, processed, packed, or distributed such drug and which thereby falsely purports or is represented to be the product of, or to have been packed or distributed by, such other drug manufacturer, processor, packer, or distributor.

(h) The term "device" (except when used in paragraph (n) of this section and in sections 331(i), 343(f), 352(c), and 362(c) of this title) means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is—

(1) recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,

(2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or

(3) intended to affect the structure or any function of the body of man or other animals, and

which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes.

(i) The term "cosmetic" means (1) articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance, and (2) articles intended for use as a component of any such articles; except that such term shall not include soap.

* * * * *

(ff) The term "dietary supplement"—

(1) means a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients:

(A) a vitamin;

(B) a mineral;

(C) an herb or other botanical;

(D) an amino acid;

(E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or

(F) a concentrate, metabolite, constituent, extract, or combination of any ingredient described in clause (A), (B), (C), (D), or (E);

(2) means a product that—

(A)(i) is intended for ingestion in a form described in section 350(c)(1)(B)(i) of this title; or

(ii) complies with section 350(c)(1)(B)(ii) of this title;

(B) is not represented for use as a conventional food or as a sole item of a meal or the diet; and

(C) is labeled as a dietary supplement; and

(3) does—

(A) include an article that is approved as a new drug under section 355 of this title, or licensed as a biologic under section 262 of Title 42, and was, prior to such approval, certification, or license, marketed as a dietary supplement or as a food unless the Secretary has issued a regulation, after notice and comment, finding that the article, when used as or in a dietary supplement under the conditions of use and dosages set forth in the labeling for such dietary supplement, is unlawful under section 342(f) of this title; and

(B) not include—

(i) an article that is approved as a new drug under section 355 of this title, certified as an antibiotic under section 357 of this title, or licensed as a biologic under section 262 of Title 42, or

(ii) an article authorized for investigation as a new drug, antibiotic, or biological for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public,

which was not before such approval, certification, licensing, or authorization marketed as a dietary supplement or as a food unless the Secretary, in the Secretary's discretion, has issued a regulation, after notice and comment, finding that the article would be lawful under this chapter.

Except for purposes of paragraph (g), a dietary supplement shall be deemed to be a food within the meaning of this chapter.

(gg) The term "processed food" means any food other than a raw agricultural commodity and includes any raw agricultural commodity that has been subject to processing, such as canning, cooking, freezing, dehydration, or milling.

§ 343. Misbranded food

A food shall be deemed to be misbranded—

* * * * *

(r) Nutrition levels and health-related claims

(1) Except as provided in clauses (A) through (C) of subparagraph (5), if it is a food intended for human consumption which is offered for sale and for which a claim is made in the label or labeling of the food which expressly or by implication—

(A) characterizes the level of any nutrient which is of the type required by paragraph (q)(1) or (q)(2) to be in the label or labeling of the food unless the claim is made in accordance with subparagraph (2), or

(B) characterizes the relationship of any nutrient which is of the type required by paragraph (q)(1) or (q)(2) of this section to be in the label or labeling of the food to a disease or a health-related condition unless the claim is made in accordance with subparagraph (3) or (5)(D).

A statement of the type required by paragraph (q) of this section that appears as part of the nutrition information required or permitted by such paragraph is not a claim which is subject to this paragraph and a claim subject to clause (A) is not subject to clause (B).

(2)(A) Except as provided in subparagraphs (4)(A)(ii) and (4)(A)(iii) and clauses (A) through (C) of subparagraph (5), a claim described in subparagraph (1)(A)—

(i) may be made only if the characterization of the level made in the claim uses terms which are defined in regulations of the Secretary,

(ii) may not state the absence of a nutrient unless—

(I) the nutrient is usually present in the food or in a food which substitutes for the food as defined by the Secretary by regulation, or

(II) the Secretary by regulation permits such a statement on the basis of a finding that such a statement would assist consumers in maintaining healthy dietary practices and the statement discloses that the nutrient is not usually present in the food,

(iii) may not be made with respect to the level of cholesterol in the food if the food contains, as determined by the Secretary by regulation, fat or saturated fat in an amount which increases to persons in the general population the risk of disease or a health related condition which is diet related unless—

(I) the Secretary finds by regulation that the level of cholesterol is substantially less than the level

usually present in the food or in a food which substitutes for the food and which has a significant market share, or the Secretary by regulation permits a statement regarding the absence of cholesterol on the basis of a finding that cholesterol is not usually present in the food and that such a statement would assist consumers in maintaining healthy dietary practices and the regulation requires that the statement disclose that cholesterol is not usually present in the food, and

(II) the label or labeling of the food discloses the level of such fat or saturated fat in immediate proximity to such claim and with appropriate prominence which shall be no less than one-half the size of the claim with respect to the level of cholesterol,

(iv) may not be made with respect to the level of saturated fat in the food if the food contains cholesterol unless the label or labeling of the food discloses the level of cholesterol in the food in immediate proximity to such claim and with appropriate prominence which shall be no less than one-half the size of the claim with respect to the level of saturated fat,

(v) may not state that a food is high in dietary fiber unless the food is low in total fat as defined by the Secretary or the label or labeling discloses the level of total fat in the food in immediate proximity to such statement and with appropriate prominence which shall be no less than one-half the size of the claim with respect to the level of dietary fiber, and

(vi) may not be made if the Secretary by regulation prohibits the claim because the claim is misleading in light of the level of another nutrient in the food.

(B) If a claim described in subparagraph (1)(A) is made with respect to a nutrient in a food and the Secretary makes a determination that the food contains a nutrient at a level that increases to persons in the general population the risk of a disease or health-related condition that is diet related, the label or labeling of such food shall contain, prominently and in immediate proximity to such claim, the following statement: "See nutrition information for _____ content." The blank shall identify the nutrient associated with the increased disease or health-related condition risk. In making the determination described in this clause, the Secretary shall take into account the significance of the food in the total daily diet.

(C) Subparagraph (2)(A) does not apply to a claim described in subparagraph (1)(A) and contained in the label or labeling of a food if such claim is contained in the brand name of such food and such brand name was in use on such food before October 25, 1989, unless the brand name contains a term defined by the Secretary under subparagraph (2)(A)(i). Such a claim is subject to paragraph (a).

(D) Subparagraph (2) does not apply to a claim described in subparagraph (1)(A) which uses the term "diet" and is contained in the label or labeling of a soft drink if (i) such claim is contained in the brand name of such soft drink, (ii) such brand name was in use on such soft drink before October 25, 1989, and (iii) the use of the term "diet" was in conformity with section 105.66 of title 21 of the Code of Federal Regulations. Such a claim is subject to paragraph (a).

(E) Subclauses (i) through (v) of subparagraph (2)(A) do not apply to a statement in the label or labeling of food which describes the percentage of vitamins and minerals in the food in relation to the amount of such vitamins and minerals recommended for daily consumption by the Secretary.

(F) Subclause (i) clause (A) does not apply to a statement in the labeling of a dietary supplement that characterizes the percentage level of a dietary ingredient for which the Secretary has not established a reference daily intake, daily recommended value, or other recommendation for daily consumption.

(G) A claim of the type described in subparagraph (1)(A) for a nutrient, for which the Secretary has not promulgated a regulation under clause (A)(i), shall be authorized and may be made with respect to a food if—

(i) a scientific body of the United States Government with official responsibility for public health protection or research directly relating to human nutrition (such as the National Institutes of Health or the Centers for Disease Control and Prevention) or the National Academy of Sciences or any of its subdivisions has published an authoritative statement, which is currently in effect, which identifies the nutrient level to which the claim refers;

(ii) a person has submitted to the Secretary, at least 120 days (during which the Secretary may notify any person who is making a claim as authorized by clause

(C) that such person has not submitted all the information required by such clause) before the first introduction into interstate commerce of the food with a label containing the claim, (I) a notice of the claim, which shall include the exact words used in the claim and shall include a concise description of the basis upon which such person relied for determining that the requirements of subclause (i) have been satisfied, (II) a copy of the statement referred to in subclause (i) upon which such person relied in making the claim, and (III) a balanced representation of the scientific literature relating to the nutrient level to which the claim refers;

(iii) the claim and the food for which the claim is made are in compliance with clauses (A) and (B), and are otherwise in compliance with paragraph (a) and section 321(n) of this title; and

(iv) the claim is stated in a manner so that the claim is an accurate representation of the authoritative statement referred to in subclause (i) and so that the claim enables the public to comprehend the information provided in the claim and to understand the relative significance of such information in the context of a total daily diet.

For purposes of this clause, a statement shall be regarded as an authoritative statement of a scientific body described in subclause (i) only if the statement is published by the scientific body and shall not include a statement of an employee of the scientific body made in the individual capacity of the employee.

(H) A claim submitted under the requirements of clause (G) may be made until—

(i) such time as the Secretary issues a regulation—

(I) prohibiting or modifying the claim and the regulation has become effective, or

(II) finding that the requirements of clause (G) have not been met, including finding that the petitioner had not submitted all the information required by such clause; or

(ii) a district court of the United States in an enforcement proceeding under chapter III has determined that the requirements of clause (G) have not been met.

(3)(A) Except as provided in subparagraph (5), a claim described in subparagraph (1)(B) may only be made—

(i) if the claim meets the requirements of the regulations of the Secretary promulgated under clause (B) and

(ii) if the food for which the claim is made does not contain, as determined by the Secretary by regulation, any nutrient in an amount which increases to persons in the general population the risk of a disease or health-related condition which is diet related, taking into account the significance of the food in the total daily diet, except that the Secretary may by regulation permit such a claim based on a finding that such a claim would assist consumers in maintaining healthy dietary practices and based on a requirement that the label contain a disclosure of the type required by subparagraph (2)(B).

(B)(i) The Secretary shall promulgate regulations authorizing claims of the type described in subparagraph (1)(B) only if the Secretary determines, based on the totality of publicly available scientific evidence (including evidence from well-designed studies conducted in a manner which is consistent with generally recognized scientific procedures and principles), that there is significant scientific agreement, among experts qualified by scientific training and experience to evaluate such claims, that the claim is supported by such evidence.

(ii) A regulation described in subclause (i) shall describe—

(I) the relationship between a nutrient of the type required in the label or labeling of food by paragraph (q)(1) or (q)(2) and a disease or health-related condition, and

(II) the significance of each such nutrient in affecting such disease or health-related condition.

(iii) A regulation described in subclause (i) shall require such claim to be stated in a manner so that the claim is an accurate representation of the matters set out in subclause (ii) and so that the claim enables the public to comprehend the information provided in the claim and to understand the relative significance of such information in the context of a total daily diet.

(C) Notwithstanding the provisions of clauses (A)(i) and (B), a claim of the type described in subparagraph (1)(B) which is not authorized by the Secretary in a regulation promulgated in accordance with clause (B) shall be authorized and may be made with respect to a food if—

(i) a scientific body of the United States Government with official responsibility for public health protection or research directly relating to human nutrition (such as the National Institutes of Health or the Centers for Disease Control and Prevention) or the National Academy of Sciences or any of its subdivisions has published an authoritative statement, which is currently in effect, about the relationship between a nutrient and a disease or health-related condition to which the claim refers;

(ii) a person has submitted to the Secretary, at least 120 days (during which the Secretary may notify any person who is making a claim as authorized by clause (C) that such person has not submitted all the information required by such clause) before the first introduction into interstate commerce of the food with a label containing the claim, (I) a notice of the claim, which shall include the exact words used in the claim and shall include a concise description of the basis upon which such person relied for determining that the requirements of subclause (i) have been satisfied, (II) a copy of the statement referred to in subclause (i) upon which such person relied in making the claim, and (III) a balanced representation of the scientific literature relating to the relationship between a nutrient and a disease or health-related condition to which the claim refers;

(iii) the claim and the food for which the claim is made are in compliance with clause (A)(ii) and are otherwise in compliance with paragraph (a) and section 321(n) of this title; and

(iv) the claim is stated in a manner so that the claim is an accurate representation of the authoritative statement referred to in subclause (i) and so that the claim enables the public to comprehend the information provided in the claim and to understand the relative significance of such information in the context of a total daily diet.

For purposes of this clause, a statement shall be regarded as an authoritative statement of a scientific body described in subclause (i) only if the statement is published by the scientific body and shall not include a statement of an employee of the scientific body made in the individual capacity of the employee.

(D) A claim submitted under the requirements of clause (C) may be made until—

(i) such time as the Secretary issues a regulation under the standard in clause (B)(i)—

(I) prohibiting or modifying the claim and the regulation has become effective, or

(II) finding that the requirements of clause (C) have not been met, including finding that the petitioner has not submitted all the information required by such clause; or

(ii) a district court of the United States in an enforcement proceeding under chapter III has determined that the requirements of clause (C) have not been met.

(4)(A)(i) Any person may petition the Secretary to issue a regulation under subparagraph (2)(A)(i) or (3)(B) relating to a claim described in subparagraph (1)(A) or (1)(B). Not later than 100 days after the petition is received by the Secretary, the Secretary shall issue a final decision denying the petition or file the petition for further action by the Secretary. If the Secretary does not act within such 100 days, the petition shall be deemed to be denied unless an extension is mutually agreed upon by the Secretary and the petitioner. If the Secretary denies the petition or the petition is deemed to be denied, the petition shall not be made available to the public. If the Secretary files the petition, the Secretary shall deny the petition or issue a proposed regulation to take the action requested in the petition not later than 90 days after the date of such decision. If the Secretary does not act within such 90 days, the petition shall be deemed to be denied unless an extension is mutually agreed upon by the Secretary and the petitioner. If the Secretary issues a proposed regulation, the rulemaking shall be completed within 540 days of the date the petition is received by the Secretary. If the Secretary does not issue a regulation within such 540 days, the Secretary shall provide the Committee on Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate the reasons action on the regulation did not occur within such 540 days.

(ii) Any person may petition the Secretary for permission to use in a claim described in subparagraph (1)(A) terms that are consistent with the terms defined by the Secretary under subparagraph (2)(A)(i). Within 90 days of the submission of such a petition, the Secretary shall issue a final decision denying the petition or granting such permission.

(iii) Any person may petition the Secretary for permission to use an implied claim described in subparagraph (1)(A) in a brand name. After publishing notice of an opportunity to com-

ment on the petition in the Federal Register and making the petition available to the public, the Secretary shall grant the petition if the Secretary finds that such claim is not misleading and is consistent with terms defined by the Secretary under subparagraph (2)(A)(i). The Secretary shall grant or deny the petition within 100 days of the date it is submitted to the Secretary and the petition shall be considered granted if the Secretary does not act on it within such 100 days.

(B) A petition under clause (A)(i) respecting a claim described in subparagraph (1)(A) or (1)(B) shall include an explanation of the reasons why the claim meets the requirements of this paragraph and a summary of the scientific data which supports such reasons.

(C) If a petition for a regulation under subparagraph (3)(B) relies on a report from an authoritative scientific body of the United States, the Secretary shall consider such report and shall justify any decision rejecting the conclusions of such report.

(5)(A) This paragraph does not apply to infant formulas subject to section 350a(h) of this title and medical foods as defined in section 360ee(b) of this title.

(B) Subclauses (iii) through (v) of subparagraph (2)(A) and subparagraph (2)(B) do not apply to food which is served in restaurants or other establishments in which food is served for immediate human consumption or which is sold for sale or use in such establishments.

(C) A subparagraph (1)(A) claim made with respect to a food which claim is required by a standard of identity issued under section 341 of this title shall not be subject to subparagraph (2)(A)(i) or (2)(B).

(D) A subparagraph (1)(B) claim made with respect to a dietary supplement of vitamins, minerals, herbs, or other similar nutritional substances shall not be subject to subparagraph (3) but shall be subject to a procedure and standard, respecting the validity of such claim, established by regulation of the Secretary.

(6) For purposes of paragraph (r)(1)(B), a statement for a dietary supplement may be made if—

> **(A)** the statement claims a benefit related to a classical nutrient deficiency disease and discloses the prevalence of such disease in the United States, describes the role of a nutrient or dietary ingredient intended to affect the structure or function in humans, characterizes the documented mechanism by which a nutrient or dietary ingredient acts to maintain such structure or function, or describes general

well-being from consumption of a nutrient or dietary ingredient,

(B) the manufacturer of the dietary supplement has substantiation that such statement is truthful and not misleading, and

(C) the statement contains, prominently displayed and in boldface type, the following: "This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

A statement under this subparagraph may not claim to diagnose, mitigate, treat, cure, or prevent a specific disease or class of diseases. If the manufacturer of a dietary supplement proposes to make a statement described in the first sentence of this subparagraph in the labeling of the dietary supplement, the manufacturer shall notify the Secretary no later than 30 days after the first marketing of the dietary supplement with such statement that such a statement is being made.

(7) The Secretary may make proposed regulations issued under this paragraph effective upon publication pending consideration of public comment and publication of a final regulation if the Secretary determines that such action is necessary—

(A) to enable the Secretary to review and act promptly on petitions the Secretary determines provide for information necessary to—

(i) enable consumers to develop and maintain healthy dietary practices;

(ii) enable consumers to be informed promptly and effectively of important new knowledge regarding nutritional and health benefits of food; or

~~**(iii)** ensure~~ that scientifically sound nutritional and health information is provided to consumers as soon as possible; or

(B) to enable the Secretary to act promptly to ban or modify a claim under this paragraph.

Such proposed regulations shall be deemed final agency action for purposes of judicial review.

(s) Dietary supplements

If—

(1) it is a dietary supplement; and

(2)(A) the label or labeling of the supplement fails to list—

(i) the name of each ingredient of the supplement that is described in section 321(ff) of this title; and

(ii)(I) the quantity of each such ingredient; or

(II) with respect to a proprietary blend of such ingredients, the total quantity of all ingredients in the blend;

(B) the label or labeling of the dietary supplement fails to identify the product by using the term "dietary supplement", which term may be modified with the name of such an ingredient;

(C) the supplement contains an ingredient described in section 321(ff)(1)(C) of this title, and the label or labeling of the supplement fails to identify any part of the plant from which the ingredient is derived;

(D) the supplement—

(i) is covered by the specifications of an official compendium;

(ii) is represented as conforming to the specifications of an official compendium; and

(iii) fails to so conform; or

(E) the supplement—

(i) is not covered by the specifications of an official compendium; and

(ii)(I) fails to have the identity and strength that the supplement is represented to have; or

(II) fails to meet the quality (including tablet or capsule disintegration), purity, or compositional specifications, based on validated assay or other appropriate methods, that the supplement is represented to meet.

~~A dietary supplement shall not be deemed~~ misbranded solely because its label or labeling contains directions or conditions of use or warnings.

§ 360ee. Grants and contracts for development of drugs for rare diseases and conditions

(a) Authority of Secretary

The Secretary may make grants to and enter into contracts with public and private entities and individuals to assist in (1) defraying the costs of qualified testing expenses incurred in connection with the development of drugs for rare diseases and conditions, (2) defraying the costs of developing medical devices for rare diseases or conditions, and (3) defraying the costs of developing medical foods for rare diseases or conditions.

(b) Definitions

For purposes of subsection (a) of this section:

(1) The term "qualified testing" means—

(A) human clinical testing—

(i) which is carried out under an exemption for a drug for a rare disease or condition under section 355(i) of this title (or regulations issued under such section); and

(ii) which occurs after the date such drug is designated under section 360bb of this title and before the date on which an application with respect to such drug is submitted under section 355(b) of this title or under section 262 of Title 42; and

(B) preclinical testing involving a drug for a rare disease or condition which occurs after the date such drug is designated under section 360bb of this title and before the date on which an application with respect to such drug is submitted under section 355(b) of this title or under section 262 of Title 42.

(2) The term "rare disease or condition" means (1) in the case of a drug, any disease or condition which (A) affects less than 200,000 persons in the United States, or (B) affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug, (2) in the case of a medical device, any disease or condition that occurs so infrequently in the United States that there is no reasonable expectation that a medical device for such disease or condition will be developed without assistance under subsection (a) of this section, and (3) in the case of a medical food, any disease or condition that occurs so infrequently in the United States that there is no reasonable expectation that a medical food for such disease or condition will be developed without assistance under subsection (a) of this section. Determinations under the preceding sentence with respect to any drug shall be made on the basis of the facts and circumstances as of the date the request for designation of the drug under section 360bb of this title is made.

(3) The term "medical food" means a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation.

(c) Authorization of appropriations

For grants and contracts under subsection (a) of this section there are authorized to be appropriated $10,000,000 for fiscal year 1988, $12,000,000 for fiscal year 1989,[1] $14,000,000 for fiscal year 1990.

Subpart E—Specific Requirements for Health Claims

§ 101.70 Petitions for health claims.

(a) Any interested person may petition the Food and Drug Administration (FDA) to issue a regulation regarding a health claim. An original and one copy of the petition shall be submitted, or the petitioner may submit an original and a computer readable disk containing the petition. Contents of the disk should be in a standard format, such as ASCII format. (Petitioners interested in submitting a disk should contact the Center for Food Safety and Applied Nutrition for details.) If any part of the material submitted is in a foreign language, it shall be accompanied by an accurate and complete English translation. The petition shall state the petitioner's post office address to which any correspondence required by section 403 of the Federal Food, Drug, and Cosmetic Act may be sent.

(b) Pertinent information may be incorporated in, and will be considered as part of, a petition on the basis of specific reference to such information submitted to and retained in the files of FDA. Such information may include any findings, along with the basis of the findings, of an outside panel with expertise in the subject area. Any reference to published information shall be accompanied by reprints, or easily readable copies of such information.

(c) If nonclinical laboratory studies are included in a petition, the petition shall include, with respect to each nonclinical study contained in the petition, either a statement that the study has been conducted in compliance with the good laboratory practice regulations as set forth in part 58 of this chapter, or, if any such study was not conducted in compliance with such regulations, a brief statement of the reason for the noncompliance.

(d) If clinical or other human investigations are included in a petition, the petition shall include a statement that they were either conducted in compliance with the requirements for institutional review set forth in part 56 of this chapter, or were not subject to such requirements in accordance with § 56.104 or § 56.105, and a statement that they

were conducted in compliance with the requirements for informed consent set forth in part 50 of this chapter.

(e) All data and information in a health claim petition are available for public disclosure after the notice of filing of petition is issued to the petitioner, except that clinical investigation reports, adverse reaction reports, product experience reports, consumer complaints, and other similar data and information shall only be available after deletion of:

(1) Names and any information that would identify the person using the product.

(2) Names and any information that would identify any third party involved with the report, such as a physician or hospital or other institution.

(f) Petitions for a health claim shall include the following data and be submitted in the following form:

(Date)_____
Name of petitioner _____
Post office address _____
Subject of the petition _____
Food and Drug Administration,
Office of Nutritional Products, Labeling and Dietary Supplements (HFS-800),
5100 Paint Branch Pkwy.,
College Park, MD 20740.

The undersigned, _____ submits this petition pursuant to section 403(r)(4) or 403(r)(5)(D) of the Federal Food, Drug, and Cosmetic Act with respect to (statement of the substance and its health claim).

Attached hereto, and constituting a part of this petition, are the following:

A. Preliminary requirements. A complete explanation of how the substance conforms to the requirements of §101.14(b) (21 CFR 101.14(b)). For petitions where the subject substance is a food ingredient or a component of a food ingredient, the petitioner should compile a comprehensive list of the specific ingredients that will be added to the food to supply the substance in the food bearing the health claim. For each such ingredient listed, the petitioner should state how the ingredient complies with the requirements of §101.14(b)(3)(ii), e.g., that its use is generally recognized as safe (GRAS), listed as a food additive, or authorized by a prior sanction issued by the agency, and what the basis is for the GRAS claim, the food additive status, or prior sanctioned status.

B. Summary of scientific data. The summary of scientific data provides the basis upon which authorizing a health claim can be justified as providing the health benefit. The summary must establish that, based on the totality of publicly available scientific evidence (including evidence from well-designed studies conducted in a manner which is consistent with generally recognized scientific procedures and principles), there is significant scientific agreement among experts qualified by scientific training and experience to evaluate such claims, that the claim is supported by such evidence.

The summary shall state what public health benefit will derive from use of the claim as proposed. If the claim is intended for a specific group within the population, the summary shall specifically address nutritional needs of such group and shall include scientific data showing how the claim is likely to assist in meeting such needs.

The summary shall concentrate on the findings of appropriate review articles, National Institutes of Health consensus development conferences, and other appropriate resource materials. Issues addressed in the summary shall include answers to such questions as:

1. Is there an optimum level of the particular substance to be consumed beyond which no benefit would be expected?

2. Is there any level at which an adverse effect from the substance or from foods containing the substance occurs for any segment of the population?

3. Are there certain populations that must receive special consideration?

4. What other nutritional or health factors (both positive and negative) are important to consider when consuming the substance?

In addition, the summary of scientific data shall include a detailed analysis of the potential effect of the use of the proposed claim on food consumption, specifically any change due to significant alterations in eating habits and corresponding changes in nutrient intake resulting from such changes in food consumption. The latter item shall specifically address the effect on the intake of nutrients that have beneficial and negative consequences in the total diet.

If the claim is intended for a significant subpopulation within the general U.S. population, the analysis shall specifically address the dietary practices of such group, and shall include data sufficient to demonstrate that the dietary analysis is representative of such group (e.g., adolescents or the elderly).

If appropriate, the petition shall explain the prevalence of the disease or health-related condition in the U.S. population and the relevance of the claim in the context of the total daily diet.

Also, the summary shall demonstrate that the substance that is the subject of the proposed claim conforms to the definition of the term "substance" in §101.14(a)(2).

C. Analytical data that show the amount of the substance that is present in representative foods that would be candidates to bear

the claim should be obtained from representative samples using methods from the Association of Official Analytical Chemists (AOAC), where available. If no AOAC method is available, the petitioner shall submit the assay method used and data establishing the validity of the method for assaying the substance in food. The validation data should include a statistical analysis of the analytical and product variability.

D. Model health claim. One or more model health claims that represent label statements that may be used on a food label or in labeling for a food to characterize the relationship between the substance in a food to a disease or health-related condition that is justified by the summary of scientific data provided in section C of the petition. The model health claim shall include:

1. A brief capsulized statement of the relevant conclusions of the summary, and

2. A statement of how this substance helps the consumer to attain a total dietary pattern or goal associated with the health benefit that is provided.

E. The petition shall include the following attachments:

1. Copies of any computer literature searches done by the petitioner (e.g., Medline).

2 Copies of articles cited in the literature searches and other information as follows:

a. All information relied upon for the support of the health claim, including copies of publications or other information cited in review articles and used to perform meta-analyses.

b. All information concerning adverse consequences to any segment of the population (e.g., sensitivity to the substance).

c. All information pertaining to the U.S. population.

F. The petitioner is required to submit either a claim for categorical exclusion under §25.30 or §25.32 of this chapter or an environmental assessment under §25.40 of this chapter.

Yours very truly,
Petitioner _____
By _____
(Indicate authority)

(g) The data specified under the several lettered headings should be submitted on separate pages or sets of pages, suitably identified. If such data have already been submitted with an earlier application from the petitioner or any other final petition, the present petition may incorporate it by specific reference to the earlier petition.

(h) The petition shall include a statement signed by the person responsible for the petition that, to the best of his/her knowledge, it is a representative and balanced submission that includes unfavorable information as well as favorable information, known to him/her to be pertinent to the evaluation of the proposed health claim.

(i) The petition shall be signed by the petitioner or by his/her attorney or agent, or (if a corporation) by an authorized official.

(j) *Agency action on the petition.* (1) Within 15 days of receipt of the petition, the petitioner will be notified by letter of the date on which the petition was received. Such notice will inform the petitioner that the petition is undergoing agency review and that the petitioner will subsequently be notified of the agency's decision to file for comprehensive review or deny the petition.

(2) Within 100 days of the date of receipt of the petition. FDA will notify the petitioner by letter that the petition has either been filed for comprehensive review or denied. The agency will deny a petition without reviewing the information contained in "B. Summary of Scientific Data" if the information in "A. Preliminary Requirements" is inadequate in explaining how the substance conforms to the requirements of §101.14(b). If the petition is denied, the notification will state the reasons therefor, including justification of the rejection of any report from an authoritative scientific body of the U.S. Government. If filed, the date of the notification letter becomes the date of filing for the purposes of this regulation. If FDA does not act within such 100 days, the petition shall be deemed to be denied unless an extension is mutually agreed upon by FDA and the petitioner. A petition that has been denied, or has been deemed to be denied, without filing will not be made available to the public. A filed petition will be available to the public to the extent provided under paragraph (e) of this section.

(3) Within 90 days of the date of filing, FDA will by letter of notification to the petitioner:

(i) Deny the petition, or

(ii) Inform the petitioner that a proposed regulation to provide for the requested use of the health claim will be published in the FEDERAL REGISTER. If the petition is denied, the notification will state the reasons therefor, including justification for the rejection of

any report from an authoritative scientific body of the U.S. Government. FDA will publish the proposal to amend the regulations to provide for the requested use of the health claim in the FEDERAL REGISTER within 90 days of the date of filing. The proposal will also announce the availability of the petition for public review.

(iii) If FDA does not act within 90 days of the date of filing, the petition shall be deemed to be denied unless an extension is mutually agreed upon by FDA and the petitioner.

(4)(i) Within 270 of the date of publication of the proposal, FDA will publish a final rule that either authorizes use of the health claim or explains why the agency has decided not to authorize one.

(ii) For cause, FDA may extend, no more than twice, the period in which it will publish a final rule; each such extension will be for no more than 90 days. FDA will publish a notice of each extension in the FEDERAL REGISTER. The document will state the basis for the extension, the length of the extension, and the date by which the final rule will be published, which date shall be within 540 days of the date of receipt of the petition.

[58 FR 2534, Jan. 6, 1993; 58 FR 17097, Apr. 1, 1993, as amended at 59 FR 425, Jan. 4, 1994; 62 FR 28232, May 22, 1997; 62 FR 40599, July 29, 1997; 63 FR 26719, May 14, 1998; 63 FR 40024, July 27, 1998; 66 FR 56035, Nov. 6, 2001]

§ 101.71 Health claims: claims not authorized.

Health claims not authorized for foods in conventional food form or for dietary supplements of vitamins, minerals, herbs, or other similar substances:

(a) Dietary fiber and cardiovascular disease.

(b) Zinc and immune function in the elderly.

[58 FR 2534, Jan. 6, 1993, as amended at 58 FR 2548, 2578, 2620, 2639, 2664, 2714, Jan. 6, 1993; 58 FR 17100, Apr. 1, 1993; 59 FR 437, Jan. 4, 1994; 65 FR 58918, Oct. 3, 2000]

§ 101.72 Health claims: calcium and osteoporosis.

(a) *Relationship between calcium and osteoporosis.* An inadequate calcium intake contributes to low peak bone mass and has been identified as one of many risk factors in the development of osteoporosis. Peak bone mass is the total quantity of bone present at maturity, and experts believe that it has the greatest bearing on whether a person will be at risk of developing osteoporosis and related bone fractures later in life. Another factor that influences total bone mass and susceptibility to osteoporosis is the rate of bone loss after skeletal maturity. An adequate intake of calcium is thought to exert a positive effect during adolescence and early adulthood in optimizing the amount of bone that is laid down. However, the upper limit of peak bone mass is genetically determined. The mechanism through which an adequate calcium intake and optimal peak bone mass reduce the risk of osteoporosis is thought to be as follows. All persons lose bone with age. Hence, those with higher bone mass at maturity take longer to reach the critically reduced mass at which bones can fracture easily. The rate of bone loss after skeletal maturity also influences the amount of bone present at old age and can influence an individual's risk of developing osteoporosis. Maintenance of an adequate intake of calcium later in life is thought to be important in reducing the rate of bone loss particularly in the elderly and in women during the first decade following menopause.

(b) *Significance of calcium.* Calcium intake is not the only recognized risk factor in the development of osteoporosis, a multifactorial bone disease. Other factors including a person's sex, race, hormonal status, family history, body stature, level of exercise, general diet, and specific life style choices such as smoking and excess alcohol consumption affect the risk of osteoporosis.

(1) Heredity and being female are two key factors identifying those individuals at risk for the development of osteoporosis. Hereditary risk factors include race: Notably, Caucasians and Asians are characterized by low peak bone mass at maturity. Caucasian women, particularly those of northern European ancestry, experience the highest incidence of osteoporosis-related bone fracture. American women

of African heritage are characterized by the highest peak bone mass and lowest incidence of osteoporotic fracture, despite the fact that they have low calcium intake.

(2) Maintenance of an adequate intake of calcium throughout life is particularly important for a subpopulation of individuals at greatest risk of developing osteoporosis and for whom adequate dietary calcium intake may have the most important beneficial effects on bone health. This target subpopulation includes adolescent and young adult Caucasian and Asian American women.

(c) *Requirements.* (1) All requirements set forth in § 101.14 shall be met.

(2) *Specific requirements*—(i) *Nature of the claim.* A health claim associating calcium with a reduced risk of osteoporosis may be made on the label or labeling of a food described in paragraph (c)(2)(ii) of this section, provided that:

(A) The claim makes clear that adequate calcium intake throughout life is not the only recognized risk factor in this multifactorial bone disease by listing specific factors, including sex, race, and age that place persons at risk of developing osteoporosis and stating that an adequate level of exercise and a healthful diet are also needed;

(B) The claim does not state or imply that the risk of osteoporosis is equally applicable to the general United States population. The claim shall identify the populations at particular risk for the development of osteoporosis. These populations include white (or the term "Caucasian") women and Asian women in their bone forming years (approximately 11 to 35 years of age or the phrase "during teen or early adult years") may be used. The claim may also identify menopausal (or the term "middle-aged") women, persons with a family history of the disease, and elderly (or "older") men and women as being at risk;

(C) The claim states that adequate calcium intake throughout life is linked to reduced risk of osteoporosis through the mechanism of optimizing peak bone mass during adolescence and early adulthood. The phrase "build and maintain good bone health" may be used to convey the concept of optimizing peak bone mass. When reference is made to persons with a family history of the disease, menopausal women, and elderly men and women, the claim may also state that adequate calcium intake is linked to reduced risk of osteoporosis through the mechanism of slowing the rate of bone loss;

(D) The claim does not attribute any degree of reduction in risk of osteoporosis to maintaining an adequate calcium intake throughout life; and

(E) The claim states that a total dietary intake greater than 200 percent of the recommended daily intake (2,000 milligrams (mg) of calcium) has no further known benefit to bone health. This requirement does not apply to foods that contain less than 40 percent of the recommended daily intake of 1,000 mg of calcium per day or 400 mg of calcium per reference amount customarily consumed as defined in § 101.12 (b) or per total daily recommended supplement intake.

(ii) *Nature of the food.* (A) The food shall meet or exceed the requirements for a "high" level of calcium as defined in § 101.54(b);

(B) The calcium content of the product shall be assimilable;

(C) Dietary supplements shall meet the United States Pharmacopeia (U.S.P.) standards for disintegration and dissolution applicable to their component calcium salts, except that dietary supplements for which no U.S.P. standards exist shall exhibit appropriate assimilability under the conditions of use stated on the product label;

(D) A food or total daily recommended supplement intake shall not contain more phosphorus than calcium on a weight per weight basis.

(d) *Optional information.* (1) The claim may include information from paragraphs (a) and (b) of this section.

(2) The claim may include information on the number of people in the United States who have osteoporosis. The sources of this information must be identified, and it must be current information from the National Center for Health Statistics, the National Institutes of Health, or "Dietary Guidelines for Americans."

(e) *Model health claim.* The following model health claims may be used in food labeling to describe the relationship between calcium and osteoporosis:

MODEL HEALTH CLAIM APPROPRIATE FOR MOST CONVENTIONAL FOODS:

Regular exercise and a healthy diet with enough calcium helps teen and young adult white and Asian women maintain good bone health and may reduce their high risk of osteoporosis later in life.

MODEL HEALTH CLAIM APPROPRIATE FOR FOODS EXCEPTIONALLY HIGH IN CALCIUM AND MOST CALCIUM SUPPLEMENTS:

Regular exercise and a healthy diet with enough calcium helps teen and young adult white and Asian women maintain good bone health and may reduce their high risk of osteoporosis later in life. Adequate calcium intake is important, but daily intakes above about 2,000 mg are not likely to provide any additional benefit.

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§ 101.75 Health claims: dietary saturated fat and cholesterol and risk of coronary heart disease.

(a) *Relationship between dietary saturated fat and cholesterol and risk of coronary heart disease.* (1) Cardiovascular disease means diseases of the heart and circulatory system. Coronary heart disease is the most common and serious form of cardiovascular disease and refers to diseases of the heart muscle and supporting blood vessels. High blood total- and low density lipoprotein (LDL)- cholesterol levels are major modifiable risk factors in the development of coronary heart disease. High coronary heart disease rates occur among people with high blood cholesterol levels of 240 milligrams/decaliter (mg/dL) (6.21 millimoles per liter (mmol/L)) or above and LDL-cholesterol levels of 160 mg/dL (4.13 mmol/L) or above. Borderline high risk blood cholesterol levels range from 200 to 239 mg/dL (5.17 to 6.18 mmol/L) and 130 to 159 mg/dL (3.36 to 4.11 mmol/L) of LDL-cholesterol. Dietary lipids (fats) include fatty acids and cholesterol. Total fat, commonly referred to as fat, is composed of saturated fat (fatty acids containing no double bonds), and monounsaturated and polyunsaturated fat (fatty acids containing one or more double bonds).

(2) The scientific evidence establishes that diets high in saturated fat and cholesterol are associated with increased levels of blood total- and LDL-cholesterol and, thus, with increased risk of coronary heart disease. Diets low in saturated fat and cholesterol are associated with decreased levels of blood total- and LDL-cholesterol, and thus, with decreased risk of developing coronary heart disease.

(b) *Significance of the relationship between dietary saturated fat and cholesterol and risk of coronary heart disease.* (1) Coronary heart disease is a major public health concern in the United States, primarily because it accounts for more deaths than any other disease or group of diseases. Early management of risk factors for coronary heart disease is a major public health goal that can assist in reducing risk of coronary heart disease. There is a continuum of mortality risk from coronary heart disease that increases with increasing levels of blood LDL-cholesterol. Individuals with high blood LDL-cholesterol are at greatest risk. A larger number of individuals with more moderately elevated cholesterol also have increased risk of coronary events; such individuals comprise a substantial proportion of the adult U.S. population. The scientific evidence indicates that reducing saturated fat and cholesterol intakes lowers blood LDL-cholesterol and risk of heart disease in most individuals. There is also evidence that reducing saturated fat and cholesterol intakes in persons with blood cholesterol levels in the normal range also reduces risk of heart disease.

(2) Other risk factors for coronary heart disease include a family history of heart disease, high blood pressure, diabetes, cigarette smoking, obesity (body weight 30 percent greater than ideal body weight), and lack of regular physical exercise.

(3) Intakes of saturated fat exceed recommended levels in many people in the United States. Intakes of cholesterol are, on average, at or above recommended levels. One of the major public health recommendations relative to coronary heart disease risk is to consume less than 10 percent of calories from saturated fat, and an average of 30 percent or less of total calories from all fat. Recommended daily cholesterol intakes are 300 mg or less per day.

(c) *Requirements.* (1) All requirements set forth in § 101.14 shall be met.

(2) *Specific requirements*—(i) *Nature of the claim.* A health claim associating diets low in saturated fat and cholesterol with reduced risk of coronary heart disease may be made on the label

or labeling of a food described in paragraph (c)(2)(ii) of this section provided that:

(A) The claim states that diets low in saturated fat and cholesterol "may" or "might" reduce the risk of heart disease;

(B) In specifying the disease, the claim uses the terms "heart disease" or "coronary heart disease;"

(C) In specifying the nutrient, the claim uses the terms "saturated fat" and "cholesterol" and lists both;

(D) The claim does not attribute any degree of risk reduction for coronary heart disease to diets low in dietary saturated fat and cholesterol; and

(E) The claim states that coronary heart disease risk depends on many factors.

(ii) *Nature of the food.* The food shall meet all of the nutrient content requirements of §101.62 for a "low saturated fat," "low cholesterol," and "low fat" food; except that fish and game meats (i.e., deer, bison, rabbit, quail, wild turkey, geese, and ostrich) may meet the requirements for "extra lean" in §101.62.

(d) *Optional information.* (1) The claim may identify one or more of the following risk factors in addition to saturated fat and cholesterol about which there is general scientific agreement that they are major risk factors for this disease: A family history of coronary heart disease, elevated blood total and LDL-cholesterol, excess body weight, high blood pressure, cigarette smoking, diabetes, and physical inactivity.

(2) The claim may indicate that the relationship of saturated fat and cholesterol to heart disease is through the intermediate link of "blood cholesterol" or "blood total- and LDL cholesterol."

(3) The claim may include information from paragraphs (a) and (b) of this section, which summarize the relationship between dietary saturated fat and cholesterol and risk of coronary heart disease, and the significance of the relationship.

(4) In specifying the nutrients, the claim may include the term "total fat" in addition to the terms "saturated fat" and "cholesterol".

(5) The claim may include information on the number of people in the United States who have coronary heart disease. The sources of this information shall be identified, and it shall be current information from the National Center for Health Statistics, the National Institutes of Health, or "Nutrition and Your Health: Dietary Guidelines for Americans," U.S. Department of Health and Human Services (DHHS) and U.S. Department of Agriculture (USDA), Government Printing Office.

(6) The claim may indicate that it is consistent with "Nutrition and Your Health: Dietary Guidelines for Americans," DHHS and USDA, Government Printing Office.

(7) The claim may state that individuals with elevated blood total- or LDL-cholesterol should consult their physicians for medical advice and treatment. If the claim defines high or normal blood total- or LDL-cholesterol levels, then the claim shall state that individuals with high blood cholesterol should consult their physicians for medical advice and treatment.

(e) *Model health claims.*The following are model health claims that may be used in food labeling to describe the relationship between dietary saturated fat and cholesterol and risk of heart disease:

(1) While many factors affect heart disease, diets low in saturated fat and cholesterol may reduce the risk of this disease;

(2) Development of heart disease depends upon many factors, but its risk may be reduced by diets low in saturated fat and cholesterol and healthy lifestyles;

(3) Development of heart disease depends upon many factors, including a family history of the disease, high blood LDL-cholesterol, diabetes, high blood pressure, being overweight, cigarette smoking, lack of exercise, and the type of dietary pattern. A healthful diet low in saturated fat, total fat, and cholesterol, as part of a healthy lifestyle, may lower blood cholesterol levels and may reduce the risk of heart disease;

(4) Many factors, such as a family history of the disease, increased blood- and LDL-cholesterol levels, high blood pressure, cigarette smoking, diabetes,

and being overweight, contribute to developing heart disease. A diet low in saturated fat, cholesterol, and total fat may help reduce the risk of heart disease; and

(5) Diets low in saturated fat, cholesterol, and total fat may reduce the risk of heart disease. Heart disease is dependent upon many factors, including diet, a family history of the disease, elevated blood LDL-cholesterol levels, and physical inactivity.

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§ 101.77 Health claims: fruits, vegetables, and grain products that contain fiber, particularly soluble fiber, and risk of coronary heart disease.

(a) *Relationship between diets low in saturated fat and cholesterol and high in fruits, vegetables, and grain products that contain fiber, particularly soluble fiber, and risk of coronary heart disease.* (1) Cardiovascular disease means diseases of the heart and circulatory system. Coronary heart disease is the most common and serious form of cardiovascular disease and refers to diseases of the heart muscle and supporting blood vessels. High blood total- and low density lipoprotein (LDL)- cholesterol levels are major modifiable risk factors in the development of coronary heart disease. High coronary heart disease rates occur among people with high blood cholesterol levels of 240 milligrams per deciliter (mg/dL) (6.21 (mmol/L)) or above and LDL-cholesterol levels of 160 mg/dL (4.13 mmol/L) or above. Borderline high risk blood cholesterol levels range from 200 to 239 mg/dL (5.17 to 6.18 mmol/L) and 130 to 159 mg/dL (3.36 to 4.11 mmol/L) of LDL-cholesterol. Dietary lipids (fats) include fatty acids and cholesterol. Total fat, commonly referred to as fat, is composed of saturated fat (fatty acids containing no double bonds), and monounsaturated and polyunsaturated fat (fatty acids containing one or more double bonds).

(2) The scientific evidence establishes that diets high in saturated fat and cholesterol are associated with increased levels of blood total- and LDL-cholesterol and, thus, with increased risk of coronary heart disease. Diets low in saturated fat and cholesterol are associated with decreased levels of blood total- and LDL-cholesterol, and thus, with decreased risk of developing coronary heart disease.

(3) Populations with relatively low blood cholesterol levels tend to have dietary patterns that are not only low in total fat, especially saturated fat and cholesterol, but are also relatively high in fruits, vegetables, and grain products. Although the specific roles of these plant foods are not yet fully understood, many studies have shown that diets high in plant foods are associated with reduced risk of coronary

heart disease. These studies correlate diets rich in fruits, vegetables, and grain products and nutrients from these diets, such as some types of fiber, with reduced coronary heart disease risk. Persons consuming these diets frequently have high intakes of dietary fiber, particularly soluble fibers. Currently, there is not scientific agreement as to whether a particular type of soluble fiber is beneficial, or whether the observed protective effects of fruits, vegetables, and grain products against heart disease are due to other components, or a combination of components, in these diets, including, but not necessarily limited to, some types of soluble fiber, other fiber components, other characteristics of the complex carbohydrate content of these foods, other nutrients in these foods, or displacement of saturated fat and cholesterol from the diet.

(b) *Significance of the relationship between diets low in saturated fat and cholesterol, and high in fruits, vegetables, and grain products that contain fiber, particularly soluble fiber, and risk of coronary heart disease.* (1) Coronary heart disease is a major public health concern in the United States, primarily because it accounts for more deaths than any other disease or group of diseases. Early management of risk factors for coronary heart disease is a major public health goal that can assist in reducing risk of coronary heart disease. There is a continuum of mortality risk from coronary heart disease that increases with increasing levels of blood LDL-cholesterol. Individuals with high blood LDL-cholesterol are at greatest risk. A larger number of individuals with more moderately elevated cholesterol also have increased risk of coronary events; such individuals comprise a substantial proportion of the adult U.S. population. The scientific evidence indicates that reducing saturated fat and cholesterol intakes lowers blood LDL-cholesterol and risk of heart disease in most individuals, including persons with blood cholesterol levels in the normal range. Additionally, consuming diets high in fruits, vegetables, and grain products, foods that contain soluble fiber, may be a useful adjunct to a low saturated fat and low cholesterol diet.

(2) Other risk factors for coronary heart disease include a family history of heart disease, high blood pressure, diabetes, cigarette smoking, obesity (body weight 30 percent greater than ideal body weight), and lack of regular physical exercise.

(3) Intakes of saturated fat exceed recommended levels in many people in the United States. Intakes of cholesterol are, on average, at or above recommended levels. Intakes of fiber-containing fruits, vegetables, and grain products are about half of recommended intake levels. One of the major public health recommendations relative to coronary heart disease risk is to consume less than 10 percent of calories from saturated fat, and an average of 30 percent or less of total calories from all fat. Recommended daily cholesterol intakes are 300 mg or less per day. Recommended total dietary fiber intakes are about 25 grams (g) daily, of which about 25 percent (about 6 g) should be soluble fiber.

(4) Current dietary guidance recommendations encourage decreased consumption of dietary fat, especially saturated fat and cholesterol, and increased consumption of fiber-rich foods to help lower blood LDL-cholesterol levels. Results of numerous studies have shown that fiber-containing fruits, vegetables, and grain products can help lower blood LDL-cholesterol.

(c) *Requirements.* (1) All requirements set forth in §101.14 shall be met.

(2) *Specific requirements*—(i) *Nature of the claim.* A health claim associating diets low in saturated fat and cholesterol and high in fruits, vegetables, and grain products that contain fiber, particularly soluble fiber, with reduced risk of heart disease may be made on the label or labeling of a food described in paragraph (c)(2)(ii) of this section, provided that:

(A) The claim states that diets low in saturated fat and cholesterol and high in fruits, vegetables, and grain products that contain fiber "may" or "might" reduce the risk of heart disease;

(B) In specifying the disease, the claim uses the following terms: "heart disease" or "coronary heart disease:"

(C) The claim is limited to those fruits, vegetables, and grains that contain fiber;

(D) In specifying the dietary fiber, the claim uses the term "fiber," "dietary fiber," "some types of dietary fiber," "some dietary fibers," or "some fibers;" the term "soluble fiber" may be used in addition to these terms;

(E) In specifying the fat component, the claim uses the terms "saturated fat" and "cholesterol;" and

(F) The claim indicates that development of heart disease depends on many factors; and

(G) The claim does not attribute any degree of risk reduction for coronary heart disease to diets low in saturated fat and cholesterol and high in fruits, vegetables, and grain products that contain fiber.

(ii) *Nature of the food.* (A) The food shall be or shall contain a fruit, vegetable, or grain product.

(B) The food shall meet the nutrient content requirements of §101.62 for a "low saturated fat," "low cholesterol," and "low fat" food.

(C) The food contains, without fortification, at least 0.6 g of soluble fiber per reference amount customarily consumed;

(D) The content of soluble fiber shall be declared in the nutrition information panel, consistent with §101.9(c)(6)(i)(A).

(d) *Optional information.* (1) The claim may identify one or more of the following risk factors for heart disease about which there is general scientific agreement: A family history of coronary heart disease, elevated blood-, total- and LDL-cholesterol, excess body weight, high blood pressure, cigarette smoking, diabetes, and physical inactivity.

(2) The claim may indicate that the relationship of diets low in saturated fat and cholesterol, and high in fruits, vegetables, and grain products that contain fiber to heart disease is through the intermediate link of "blood cholesterol" or "blood total- and LDL-cholesterol."

(3) The claim may include information from paragraphs (a) and (b) of this section, which summarize the relationship between diets low in saturated fat and cholesterol and high in fruits, vegetables, and grain products that contain fiber and coronary heart disease, and the significance of the relationship.

(4) In specifying the nutrients, the claim may include the term "total fat" in addition to the terms "saturated fat" and "cholesterol."

(5) The claim may indicate that it is consistent with "Nutrition and Your Health: Dietary Guidelines for Americans," U.S. Department of Agriculture (USDA) and Department of Health and Human Services (DHHS), Government Printing Office (GPO).

(6) The claim may state that individuals with elevated blood total- and LDL-cholesterol should consult their physicians for medical advice and treatment. If the claim defines high or normal blood total- and LDL-cholesterol levels, then the claim shall state that individuals with high blood cholesterol should consult their physicians for medical advice and treatment.

(7) The claim may include information on the number of people in the United States who have heart disease. The sources of this information shall be identified, and it shall be current information from the National Center for Health Statistics, the National Institutes of Health, or "Nutrition and Your Health: Dietary Guidelines for Americans," USDA and DHHS, GPO.

(e) *Model health claims.* The following model health claims may be used in food labeling to characterize the relationship between diets low in saturated fat and cholesterol and high in fruits, vegetables, and grain products that contain soluble fiber:

(1) Diets low in saturated fat and cholesterol and rich in fruits, vegetables, and grain products that contain some types of dietary fiber, particularly soluble fiber, may reduce the risk of heart disease, a disease associated with many factors.

(2) Development of heart disease depends on many factors. Eating a diet low in saturated fat and cholesterol and high in fruits, vegetables, and grain products that contain fiber may lower blood cholesterol levels and reduce your risk of heart disease.

[58 FR 2578, Jan. 6, 1993]